

DOCUMENT-IDENTIFIER: US 20080153773 A1

TITLE: MODULATORS OF PHOSPHOTYROSYL PHOSPHATASE ACTIVATOR

----- KWIC -----

Description of Disclosure - DETX (77):

[0093]Embodiments of the invention also include methods for treating a patient having a condition characterized by aberrant cell growth wherein administration of a therapeutically effective amount of an ATPase inhibitor is administered to the patient, and the ATPase inhibitor binds to PTPA inducing apoptosis within the area of the patient exhibiting aberrant cell growth. The method may further include the concurrent administration a chemotherapeutic agent, such as, but not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

Description of Disclosure - DETX (81):

[0097]Embodiments of the invention also include a method of treating a patient with cancer or an autoimmune disease by promoting apoptosis wherein administration of a therapeutically effective amount of ATPase inhibitors, and the ATPase inhibitor binds to PTPA inhibiting the activation of the phosphotyrosyl activity of PP2A. The method may further include concurrent administration of a chemotherapeutic agent including, but not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

DOCUMENT-IDENTIFIER: US 20080138280 A1

TITLE: Composition and Methods For Inhibiting Cell Survival

----- KWIC -----

Description of Disclosure - DETX (37):

[0051]In addition to cytokines, other chemotherapeutic agents are suitable, including but are not limited the chemotherapeutic agents described in "Modern Pharmacology with Clinical Applications", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (2004), herein incorporated by reference. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors: CPF (8-Cyclopentyl-1,3-dimethylxanthine, topoisomerase I inhibitor) and VP16 (etoposide, topoisomerase II inhibitor).

Claims Text - CLTX (3):

3. The therapeutic composition of claim 2, wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Claims Text - CLTX (9):

9. The therapeutic composition of claim 2, wherein the chemopotentiating agent is nitrosylcobalamin and wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-strogenic analogs.

Claims Text - CLTX (16):

16. The therapeutic composition of claim 14, wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Claims Text - CLTX (21):

21. The method of claim 20, wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Claims Text - CLTX (32):

32. The method of claim 30, wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal antiestrogenic analogs.

Claims Text - CLTX (34):

34. The method of claim 30, wherein the chemopotentiating agent is nitrosylcobalamin and wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Claims Text - CLTX (41):

41. The method of claim 39, wherein the chemotherapeutic agent is selected from the group consisting of alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

DOCUMENT-IDENTIFIER: US 20080124535 A1

TITLE: Surface-Structured Substrate And Production Thereof

----- KWIC -----

Brief Summary Text - BSTX (38):

[0045]According to a further preferred embodiment the substrate material applied in step (b) can be functionalized before or after the hardening with heterobifunctional molecules for the binding of further molecules. The heterobifunctional molecule is constructed in such a manner that it has at least two different functional groups. At least one of these functional groups is such that it can bind to the hardenable material of the second substrate while the chemical functionality of the other functional group(s) remains preserved even after the binding. For example, 2-carboxyethylacrylate, propenethiol and 2-aminoethylmethacrylate are suitable for this. Thus, e.g., a biofunctionalization of the remaining substrate surface can be carried out with any biologically interesting molecules in addition to the biofunctionalization of the nanostructure. In this connection growth factors such as EGF, NGF and TGF as well as cellular adhesion proteins and/or peptides such as fibronectin, RGD and catherines as well as extracellular signal molecules such as vasopressin, interferon, insulin are especially interesting here. Molecules of different types can be fixed adjacent to each other in an ordered manner with such a functionalization, so that they enter into a regulated interaction with each other. For example, a PEG hydrogel into which carboxyl groups are bound during the polymerization can be activated with the growth factor EGF while in addition the nanostructures are functionalized as described above with RGD for cell binding, which can be used, e.g., for serum-free cell cultures. Another example is the geometric arrangement of viral spike proteins on the nanostructures with a functionalization of the hydrogel with cellular growth factors.

DOCUMENT-IDENTIFIER: US 20080063653 A1

TITLE: Human Cytotoxic T-Lymphocyte Epitope and Its Agonist
Epitope From the Non-Variable Number of Tandem Repeat
Sequence of Muc-1

----- KWIC -----

Description of Disclosure - DETX (229):

[0226]A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art. Briefly, ex vivo culture and expansion comprises: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a subject from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20080058247 A1

TITLE: Polynucleotides and Polypeptides Encoding Receptors

----- KWIC -----

Brief Summary Text - BSTX (12):

[0013] Moreover, the EGFR family of plasma membrane proteins are an integral component of normal cellular proliferation and in the pathogenesis of the cancerous state. The family is relatively small and includes the EGFR, .alpha.-erbB-2, c-erbB-3, and others. Various cancers are correlated with aberrant expression of one or more of these genes. A number of ligands have been identified which bind to the EGFR-like receptors listed above including TGF-a, heparin-binding EGF, amphiregulin, criptoregulin, heregulin, and others. A large fraction of adenocarcinomas examined to date, especially those of the breast, colon, and pancreas, are typified by the amplification or overexpression of the c-erbB-2 gene. EGF, or an analogous ligand, initiates the cellular growth factor response by binding to the EGFR, or EGFR-related, receptor. Following the binding event, the receptor molecule dimerizes activating its intracellular tyrosine kinase domain. This event results in the phosphorylation of specific tyrosine residues near the carboxy terminus of the receptor. The diversity of signals able to be transduced through the relatively small number of EGFR-related receptor molecules is amplified considerably by the recent finding that EGFR-like receptor molecules can function when dimerized with other EGFR family members forming heterodimers.

DOCUMENT-IDENTIFIER: US 20080058223 A1

TITLE: PASSAGED NEURAL STEM CELL-DERIVED NEURONAL NETWORKS AS
SENSING ELEMENTS FOR DETECTION OF ENVIRONMENTAL THREATS

----- KWIC -----

Description of Disclosure - DETX (16):

[0024] Optionally, while the neural network is maintained in the serum-free medium, at least one compound may be added to promote and up-regulate cellular differentiation. In a preferred embodiment, the compound is a cellular growth factor, more preferably a neurotrophin, and most preferably a brain-derived neurotrophic factor (BDNF).

DOCUMENT-IDENTIFIER: US 20080039486 A1

TITLE: PRODUCTION OF POLYKETIDES AND OTHER NATURAL PRODUCTS

----- KWIC -----

Description of Disclosure - DETX (321):

[0478] Alarcon, C. M., Heitman, J., and Cardenas, M. E. (1999) Protein kinase activity and identification of a toxic effector domain of the target of rapamycin TOR proteins in yeast. *Molecular Biology of the Cell* 10: 2531-2546. [0479] Aparicio, J. F., Molnar, I., Schwecke, T., Konig, A., Haydock, S. F., Khaw, L. E., Staunton, J., and Leadlay, P. F. (1996) Organization of the biosynthetic gene cluster for rapamycin in *Streptomyces hygroscopicus*: analysis of the enzymatic domains in the modular polyketide synthase. *Gene* 169: 9-16. [0480] Baker, H., Sidorowicz, A., Sehgal, S. N., and Vezina, C. (1978) Rapamycin (AY-22,989), a new antifungal antibiotic. III. In vitro and in vivo evaluation. *Journal of Antibiotics* 31: 539-545. [0481] Bierman, M., Logan, R., O'Brien, K., Seno, E. T., Nagaraja Rao, R., and Schoner, B. E. (1992) Plasmid cloning vectors for the conjugal transfer of DNA from *Escherichia coli* to *Streptomyces* spp. *Gene* 116: 4349. [0482] Blanc, V., Lagneaux, D., Didier, P., Gil, P., Lacroix, P., and Crouzet, J. (1995) Cloning and analysis of structural genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the conversion of pristinamycin II.sub.B to pristinamycin II.sub.A (PII.sub.A): PII.sub.A synthase and NADH:riboflavin 5'-phosphate oxidoreductase. *Journal of Bacteriology* 177: 5206-5214. [0483] Blanc, V., Gil, P., Bamas-Jacques, N., Lorenzon, S., Zagorec, M., Schleuniger, J., Bisch, D., Blanche, F., Debussche, L., Crouzet, J., and Thibaut, D. (1997) Identification and analysis of genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the biosynthesis of the 4-dimethylamino-L-phenylalanine precursor of pristinamycin I. *Molecular Microbiology* 23: 191-202. [0484] Box, S. J., Shelley, P. R., Tyler, J. W., Verrall, M. S., Warr, S. R. C., Badger, A. M., Levy, M. A., and Banks, R. M. (1995) 27-O-Demethylrapamycin, an immunosuppressant compound produced by a new strain of *Streptomyces hygroscopicus*. *Journal of Antibiotics* 48:1347-1349. [0485] Brown, E. J., Albers, M. W., Shin, T. B., Ichikawa, K., Keith, C. T., Lane, W. S., and Schreiber, S. L. (1994) A mammalian protein targeted by G1-arresting rapamycin-receptor complex. *Nature* 369: 756-758. [0486] Brunn, G. J., Williams, J., Sabers, C., Wiederrecht, G., Lawrence, J. C., and Abraham, R. T. (1996) Direct inhibition of the signaling functions of the mammalian target of rapamycin by the phosphoinositide 3-kinase inhibitors, wortmannin and LY294002. *EMBO Journal* 15: 5256-5267. [0487] Cao, W., Mohacsi, P., Shorthouse, R., Pratt, R. and Morris, R. E. (1995). Effects of rapamycin on growth factor-stimulated vascular smooth muscle cell DNA synthesis. Inhibition of basic fibroblast growth factor and platelet-derived growth factor action and antagonism of rapamycin by FK506. *Transplantation* 59(3):390-395. [0488] Carlson, R. P., Hartman, D. A., Tomchek, L. A., Walter, T. L., Lugay, J. R., Calhoun, W., Sehgal, S. N., Chang, J. Y. (1993). Rapamycin, a potential

disease-modifying antiarthritic drug. *J. Pharmacol. Exp. Ther.* 266(2):1125-38. [0489] Chambrault, B., Radanyi, C., Camonis, J. H., Shazand, K., Rajkowski, K., and Baulieu, E. E. (1996) FAP48, a new protein that forms specific complexes both immunophilins FKBP59 and FKBP12. Prevention by the immunosuppressant drugs FK506 and rapamycin. *Journal of Biological Chemistry* 271: 32923-32929. [0490] Chang, J. Y., Sehgal, S. N., and Bansbach, C. C. (1991) FK506 and rapamycin: novel pharmacological probes of the immune response. *Trends in Pharmacological Sciences* 12: 218-223. [0491] Chen, J., Zheng, X. F., Brown, E. J., and Schreiber, S. L. (1995) Identification of an 11-kDa FKBP12-rapamycin-binding domain within the 289-kDa FKBP12-rapamycin-associated protein and characterization of a critical serine residue. *Proceedings of the National Academy of Sciences of the United States of America* 92: 4947-4951. [0492] Chini, M., Crotti, P., Gardelli, C., and Macchia, F., (1992), *Tetrahedron*, 48, 3805-3812 [0493] Choi, J. W., Chen, J., Schreiber, S. L., and Clardy, J. (1996) Structure of the FKBP12-rapamycin complex interacting with the binding domain of human FRAP. *Science* 273: 239-242. [0494] Chung, L., Liu, L., Patel, S., Carney, J. R., and Reeves, C. D. (2001) Deletion of rapQNM1 from the rapamycin gene cluster of *Streptomyces hygroscopicus* gives production of the 16-O-desmethyl-27-desmethoxy analog. *Journal of Antibiotics* 54: 250-256. [0495] Corey, E. J. and Huang, H., (1989) *Tetrahedron Lett.*, 30, 5235-5238 [0496] DiLella, A. G., and Craig, R. J. (1991) Exon organization of the human FKBP-12 gene: correlation with structural and functional protein domains. *Biochemistry* 30: 8512-8517. [0497] Du, L. C., Sanchez, C., Chen, M., Edwards, D. J., and Shen, B. (2000) The biosynthetic gene cluster for the antitumor drug bleomycin from *Streptomyces verticillus* ATCC15003 supporting functional interactions between nonribosomal peptide synthetases and a polyketide synthase. *Chemistry & Biology* 7: 623-642. [0498] Dudkin, L., Dilling, M. B., Cheshire, P. J., Harwood, F. C., Hollingshead, M., Arbuck, S. G., Travis, R., Sausville, E. A., Houghton, P. J. (2001). Biochemical correlates of mTOR inhibition by the rapamycin ester CCI-779 and tumor growth inhibition. *Clin. Cancer Res.* 7(6):1758-64 [0499] Fehr, T., Sanglier, J-J., Schuler, W., Gschwind, L, Ponelle, M., Schilling, W., Wioland, C. (1996). Antascomicin A, B, C, D and E: Novel FKBP12 binding compounds from a *Micromonospora* strain. *J. Antibiot.* 49(3): 230-233. [0500] Ferrari, S., Pearson, R. B., Siegmann, M., Kozma, S. C., and Thomas, G. (1993) The immunosuppressant rapamycin induces inactivation of p70.s6k through dephosphorylation of a novel set of sites. *Journal of Biological Chemistry* 268: 16091-16094. [0501] Findlay J. A, and Radics, L. (1980) *Canadian Journal of Chemistry* 58:579. [0502] Fishbein, T. M., Florman, S., Gondolesi, G., Schiano, T., LeLeiko, N., Tschernia, A., Kaufman, S. (2002). Intestinal transplantation before and after the introduction of sirolimus. *Transplantation*. 73(10):1538-42. [0503] Foey, A., Green, P., Foxwell, B., Feldmann, M., Brennan, F. (2002). Cytokine-stimulated T cells induce macrophage IL-10 production dependent on phosphatidylinositol 3-kinase and p70S6K: implications for rheumatoid arthritis. *Arthritis Res.* 4(1):64-70. Epub 2001 Oct. 10. [0504] Gaisser, S., Reather, J., Wirtz, G., Kellenberger, L., Staunton, J., and Leadlay, P. F. (2000) A defined system for hybrid macrolide biosynthesis in *Saccharopolyspora erythraea*. *Molecular Microbiology* 36: 391-401. [0505] Gaisser, S., Lill, R., Staunton, J., Mendez, C., Salas,

J., Leadlay, P F. (2002) Parallel pathways for oxidation of 14-membered polyketide macrolactones in *Saccharopolyspora erythraea*. *Mol Microbiol* 44:771-81. [0506] Galat, A. (2000) Sequence diversification of the FK506-binding proteins in several different genomes. *European Journal of Biochemistry* 267: 4945-4959. [0507] Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular growth factor and cytokine response in injured vessels. *Transplantation* 55(6):1409-1418. [0508] Gregory M A, Till R, Smith, M C M. (in Press) Integration site for *Streptomyces* phage .phi.BT1 and the development of site-specific integrating vectors. *J Bacteriol.* [0509] Guba, M., von Breitenbuch, P., Steinbauer, M., Koehl, G., Flegel, S., Hornung, M., Bruns, C. J., Zuelke, C., Farkas, Anthuber, M., Jauch, K. W., and Geissler, E. K. (2002) Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. *Nature Medicine* 8: 128-135. [0510] Hamilton, G. S., and Steiner, J. P. (1998) Immunophilins: Beyond immunosuppression. *Journal of Medicinal Chemistry* 41: 5119-5143. [0511] Hara, K., Yonezawa, K., Kozlowski, M. T., Sugimoto, T., Andrabi, K., Weng, Q. P., Kasuga, M., Nishimoto, I., and Avruch, J. (1997) Regulation of eIF-4E BP1 phosphorylation by mTOR. *Journal of Biological Chemistry* 272: 26457-26463. [0512] Hardwick, J. S., Kuruvilla, F. G., Tong, J. K., Shamji, A. F., and Schreiber, S. L. (1999) Rapamycin-modulated transcription defines the subset of nutrient-sensitive signaling pathways directly controlled by the Tor proteins. *Proceedings of the National Academy of Sciences of the United States of America* 96: 14866-14870. [0513] Hatanaka, H., Kino, T., Miyata, S., Inamura, N., Kuroda, A., Goto, T., Tanaka, H., Okuhara, M. (1988). FR-900520 and FR-900523, novel immunosuppressants isolated from a *Streptomyces*. II. Fermentation, isolation and physico-chemical and biological characteristics. *J. Antibiot.* (Tokyo). 41(11):1592-601. [0514] Hatanaka H, Kino T, Asano M, Goto T, Tanaka H, Okuhara M. (1989). FK-506 related compounds produced by *Streptomyces tsukubaensis* No. 9993. *J. Antibiot.* (Tokyo). 42(4):620-2 [0515] Hendrickson, B. A., Zhang, W., Craig, R. J., Jin, Y. J., Bierer, B. E., Burakoff, S., and DiLella, A. G. (1993) Structural organization of the genes encoding human and murine FK506-binding protein (FKBP)13 and comparison to FKBP1. *Gene* 134: 271-275. [0516] Hentges, K. E., Sirry, B., Gingeras, A. C., Sarbassov, D., Sonenberg, N., Sabatini, D., and Peterson, A. S. (2001) FRAP/mTOR is required for proliferation and patterning during embryonic development in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 98: 13796-13801. [0517] Hopwood, D. A. (1997) Genetic contributions to understanding polyketide synthases. *Chemical Reviews* 97: 2465-2497. [0518] Hosted, T. J., and Baltz, R. H. (1997) Use of rpsL for dominance selection and gene replacement in *Streptomyces roseosporus*. *Journal of Bacteriology* 179: 180-186. [0519] Hung, D. T., and Schreiber, S. L. (1992) cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein. *Biochemical and Biophysical Research Communications* 184: 733-738. [0520] Hung, D. T., Jamison, T. F., and Schreiber, S. L. (1996) Understanding and controlling the cell cycle with natural products. *Chemistry & Biology* 3: 623-639. [0521] Jain, S., Bicknell, G. R., Whiting, P. H., Nicholson, M. L. (2001). Rapamycin reduces expression of fibrosis-associated genes in an experimental model of renal ischaemia

reperfusion Injury. *Transplant Proc.* 33(1-2):556-8. [0522] Jin, Y. J., Burakoff, S. J., and Bierer, B. E. (1992) Molecular cloning of a 25 kDa high affinity rapamycin binding protein, FKBP25. *Journal of Biological Chemistry* 267:10942-10945. [0523] Kahan, B. D., Chang, J. Y., and Sehgal, S. N. (1991) Preclinical evaluation of a new potent immunosuppressive agent, rapamycin. *Transplantation* 52: 185-191. [0524] Kahan, B. D., and Camardo, J. S. (2001) Rapamycin: Clinical results and future opportunities. *Transplantation* 72:1181-1193. [0525] Kallen, J. A., Sedrani, R., and Cottens S. (1996) X-ray crystal structure of 28-O-methylrapamycin complexed with FKBP12: Is the cyclohexyl moiety part of the effector domain of rapamycin? *Journal of the American Chemical Society* 118: 5857-5861. [0526] Kawasome, H., Papst, P., Webb, S., Keller, G. M., Johnson, G. L., Gelfand, E. W., and Terada, N. (1998) Targeted disruption of p70^{sup.s6k} defines its role in protein synthesis and rapamycin sensitivity. *Proceedings of the National Academy of Sciences of the United States of America* 95: 5033-5038. [0527] Khaw, L. E., Bohm, G. A., Metcalfe, S., Staunton, J., and Leadlay, P. F. (1998) Mutational biosynthesis of novel rapamycins by a strain of *Streptomyces hygroscopicus* NRRL 5491 disrupted in rapL, encoding a putative lysine cyclodeaminase. *Journal of Bacteriology* 180: 809-814. [0528] Kieser, T., Bibb, M. J., Buttner, M. J., Chater, K. F., and Hopwood, D. A. (2000) *Practical Streptomyces Genetics*, John Innes Foundation, Norwich. [0529] Kirby, B., and Griffiths, C. E. M. (2001) Psoriasis: the future. *British Journal of Dermatology* 144:37-43. [0530] Kirchner, G. I., Winkler, M., Mueller L., Vidal, C., Jacobsen, W., Franzke, A., Wagner, S., Blick, S., Manns M. P., and Sewing K.-F. (2000) Pharmacokinetics of SDZ RAD and cyclosporin including their metabolites in seven kidney graft patients after the first dose of SDZ RAD. *British Journal of Clinical Pharmacology* 60:449-454. [0531] Konig, A., Schwecke, T., Molnar, I., Bohm, G., Lowden, P. A. S., Staunton, J., and Leadlay, P. F. (1997) The pipecolate-incorporating enzyme for the biosynthesis of the immunosuppressant rapamycin. Nucleotide sequence analysis, disruption and heterologous expression of rapP from *Streptomyces hygroscopicus*. *European Journal of Biochemistry* 247: 526-534. [0532] Kunz, J., Loeschmann, A., Deuter-Reinhard, M., and Hall, M. N. (2000) FAP1, a homologue of human transcription factor NF-XI, competes with rapamycin for binding to FKBP12 in yeast. *Molecular Microbiology* 37: 1480-1493. [0533] Kuo, C. J., Chung, J. K., Fiorentino, D. F., Flanagan, W. M., Blenis, J., and Crabtree, G. R. (1992) Rapamycin selectively inhibits interleukin-2 activation of p70 S6 kinase. *Nature* 358: 7073. [0534] Lee, M. H. Pascopella, L., Jacobs, W. R., Jr and Hatfull, G F. (1991). Site specific integration of mycobacteriophage L5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis* and *Bacille Calmette-Guerin*. *Proc. Natl. Acad. Sci. USA*, 88:3111-3115. [0535] Lee M H, Pascopella L, Jacobs W R Jr, Hatfull G F. (1991), Site-specific integration of mycobacteriophage L.sub.5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis*, and *bacille Calmette-Guerin*. *Proc Natl Acad Sci U S A.*; 88:3111-5. [0536] Liang, J., Choi, J., and Clardy, J. (1999) Refined structure of the FKBP12-rapamycin-FRB ternary complex at 2.2 Å resolution. *Acta Crystallographica Section D-Biological Crystallography* 55: 736-744. [0537] Lomovskaya, N., Fonstein, L., Ruan, X., Stassi, D., Katz, L., and Hutchinson, C. R. (1997) Gene disruption and replacement in the

rapamycin-producing *Streptomyces hygroscopicus* strain ATCC 29253. Microbiology-Uk 143: 875-883. [0538] Lowden, P. A. S., Bohm, G., Staunton, J., and Leadlay, P. F. (1996) The nature of the starter unit for the rapamycin polyketide synthase. Angewandte Chemie 35: 2249-2251. [0539] Lowden, P. A. S., (1997) Ph.D. Dissertation, University of Cambridge. "Studies on the biosynthesis of rapamycin". [0540] Lowden, P. A. S., Wilkinson, B., Bohm, G. A., Handa, S., Floss, H. G., Leadlay, P. F., and Staunton, J. (2001) Origin and true nature of the starter unit for the rapamycin polyketide synthase. Angewandte Chemie-International Edition 40: 777-779. [0541] Luengo, J. I., Yamashita, D. S., Dunnington, D., Beck, A. K., Rozamus, L. W., Yen, H. K., Bossard, M. J., Levy, M. A., Hand, A., Newmantarr, T., Badger, A., Faucette, L., Johnson, R. K., Dalessio, K., Porter, T., Shu, A. Y. L., Heys, R., Choi, J. W., Kongsaree, P., Clardy, J., and Holt, D. A. (1995) Structure-Activity Studies of Rapamycin Analogs

DOCUMENT-IDENTIFIER: US 20080021211 A1

TITLE: PRODUCTION OF POLYKETIDES AND OTHER NATURAL PRODUCTS

----- KWIC -----

Description of Disclosure - DETX (342):

[0471] Du, L. C., Sanchez, C., Chen, M., Edwards, D. J., and Shen, B. (2000) The biosynthetic gene cluster for the antitumor drug bleomycin from *Streptomyces verticillus* ATCC15003 supporting functional interactions between nonribosomal peptide synthetases and a polyketide synthase. *Chemistry & Biology* 7: 623-642. [0472] Dudkin, L., Dilling, M. B., Cheshire, P. J., Harwood, F. C., Hollingshead, M., Arbuck, S. G., Travis, R., Sausville, E. A., Houghton, P. J. (2001). Biochemical correlates of mTOR inhibition by the rapamycin ester CCI-779 and tumor growth inhibition. *Clin. Cancer Res.* 7(6):1758-64 [0473] Fehr, T., Sanglier, J-J., Schuler, W., Gschwind, L, Ponellei, M., Schilling, W., Wioland, C. (1996). Antascomicinc A, B, C, D and E: Novel FKBP12 binding compounds from a *Micromonospora* strain. *J. Antibiot.* 49(3): 230-233. [0474] Ferrari, S., Pearson, R. B., Siegmann, M., Kozma, S. C., and Thomas, G. (1993) The immunosuppressant rapamycin induces inactivation of p70.sup.s6k through dephosphorylation of a novel set of sites. *Journal of Biological Chemistry* 268: 16091-16094. [0475] Findlay J. A, and Radics, L. (1980) *Canadian Journal of Chemistry* 58:579. [0476] Fishbein, T. M., Florman, S., Gondolesi, G., Schiano, T., LeLeiko, N., Tschernia, A., Kaufman, S. (2002). Intestinal transplantation before and after the introduction of sirolimus. *Transplantation.* 73(10):1538-42. [0477] Foey, A., Green, P., Foxwell, B., Feldmann, M., Brennan, F. (2002). Cytokine-stimulated T cells induce macrophage IL-10 production dependent on phosphatidylinositol 3-kinase and p70S6K: implications for rheumatoid arthritis. *Arthritis Res.* 4(1):64-70. Epub 2001 Oct. 10. [0478] Gaisser, S., Reather, J., Wirtz, G., Kellenberger, L., Staunton, J., and Leadlay, P. F. (2000) A defined system for hybrid macrolide biosynthesis in *Saccharopolyspora erythraea*. *Molecular Microbiology* 36: 391-401. [0479] Gaisser, S., Lill, R., Staunton, J., Mendez, C., Salas, J., Leadlay, P F. (2002) Parallel pathways for oxidation of 14-membered polyketide macrolactones in *Saccharopolyspora erythraea*. *Mol Microbiol* 44:771-81. [0480] Galat, A. (2000) Sequence diversification of the FK506-binding proteins in several different genomes. *European Journal of Biochemistry* 267: 4945-4959. [0481] Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular growth factor and cytokine response in injured vessels. *Transplantation* 55(6):1409-1418. [0482] Gregory M A, Till R, Smith, M C M. (in Press) integration site for *Streptomyces* phage .PHI.BT1 and the development of site-specific integrating vectors. *J. Bacteriol.* Guba, M., von Breitenbuch, P., Steinbauer, M., Koehl, G., Flegel, S., Hornung, M., Bruns, C. J., Zuelke, C., Farkas, S., Anthuber, M., Jauch, K. W., and Geissler, E. K. (2002) Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis:

involvement of vascular endothelial growth factor. *Nature Medicine* 8: 128-135.

[0483] Hamilton, G. S., and Steiner, J. P. (1998) Immunophilins: Beyond immunosuppression. *Journal of Medicinal Chemistry* 41: 5119-5143. [0484] Hara, K., Yonezawa, K., Kozlowski, M. T., Sugimoto, T., Andrabi, K., Weng, Q. P., Kasuga, M., Nishimoto, I., and Avruch, J. (1997) Regulation of eIF-4E BP1 phosphorylation by mTOR. *Journal of Biological Chemistry* 272: 26457-26463.

[0485] Hardwick, J. S., Kuruvilla, F. G., Tong, J. K., Shamji, A. F., and Schreiber, S. L. (1999) Rapamycin-modulated transcription defines the subset of nutrient-sensitive signaling pathways directly controlled by the Tor proteins. *Proceedings of the National Academy of Sciences of the United States of America* 96: 14866-14870. [0486] Hatanaka, H., Kino, T., Miyata, S., Inamura, N., Kuroda, A., Goto, T., Tanaka, H., Okuhara, M. (1988). FR-900520 and FR-900523, novel immunosuppressants isolated from a *Streptomyces*. II. Fermentation, isolation and physico-chemical and biological characteristics. *J. Antibiot.* (Tokyo). 41(11):1592-601. [0487] Hatanaka H, Kino T, Asano M, Goto T, Tanaka H, Okuhara M. (1989). FK-506 related compounds produced by *Streptomyces tsukubaensis* No. 9993. *J. Antibiot.* (Tokyo). 42(4):620-2 [0488] Hendrickson, B. A., Zhang, W., Craig, R. J., Jin, Y. J., Bierer, B. E., Burakoff, S., and DiLella, A. G. (1993) Structural organization of the genes-encoding human and murine FK506-binding protein (FKBP)13 and comparison to FKBP1. *Gene* 134: 271-275. [0489] Hentges, K. E., Sirry, B., Gingeras, A. C., Sarbassov, D., Sonenberg, N., Sabatini, D., and Peterson, A. S. (2001) FRAP/mTOR is required for proliferation and patterning during embryonic development in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 98: 13796-13801. [0490] Hopwood, D. A. (1997) Genetic contributions to understanding polyketide synthases. *Chemical Reviews* 97: 2465-2497. [0491] Hosted, T. J., and Baltz, R. H. (1997) Use of rpsL for dominance selection and gene replacement in *Streptomyces roseosporus*. *Journal of Bacteriology* 179: 180-186. [0492] Hung, D. T., and Schreiber, S. L. (1992) cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein. *Biochemical and Biophysical Research Communications* 184: 733-738. [0493] Hung, D. T., Jamison, T. F., and Schreiber, S. L. (1996) Understanding and controlling the cell cycle with natural products. *Chemistry & Biology* 3: 623-639. [0494] Jain, S., Bicknell, G. R., Whiting, P. H., Nicholson, M. L. (2001). Rapamycin reduces expression of fibrosis-associated genes in an experimental model of renal ischaemia reperfusion injury. *Transplant Proc.* 33(1-2):556-8. [0495] Jin, Y. J., Burakoff, S. J., and Bierer, B. E. (1992) Molecular cloning of a 25 kDa high affinity rapamycin binding protein, FKBP25. *Journal of Biological Chemistry* 267:10942-10945. [0496] Kahan, B. D., Chang, J. Y., and Sehgal, S. N. (1991) Preclinical evaluation of a new potent immunosuppressive agent, rapamycin. *Transplantation* 52: 185-191. [0497] Kahan, B. D., and Camardo, J. S. (2001) Rapamycin: Clinical results and future opportunities. *Transplantation* 72:1181-1193. [0498] Kallen, J. A., Sedrani, R., and Cottens S. (1996) X-ray crystal structure of 28-O-methylrapamycin complexed with FKBP12: Is the cyclohexyl moiety part of the effector domain of rapamycin? *Journal of the American Chemical Society* 118: 5857-5861.

DOCUMENT-IDENTIFIER: US 20080021066 A1

TITLE: IAP INHIBITORS

----- KWIC -----

Description of Disclosure - DETX (136):

[0174] Embodiments of the invention also include a method of treating a patient with a condition in need thereof wherein administration of a therapeutically effective amount of a Smac peptidomimetic is delivered to the patient, and the Smac peptidomimetic binds to at least one IAP. In one embodiment the IAP can be XIAP. In another embodiment the IAP can be ML-IAP. In another embodiment the IAP can cIAP-1 or cIAP-2. In a further embodiment the SAP can be multiple IAP types. The method may further include the concurrent administration of another chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

Description of Disclosure - DETX (140):

[0178] Embodiments of the invention also include a method of treating a patient with cancer by promoting apoptosis wherein administration of a therapeutically effective amount of a Smac peptidomimetic, and the Smac peptidomimetic binds to at least one IAP. In one embodiment the IAP can be XIAP. In another embodiment the IAP can be ML-IAP. In another embodiment the IAP can cIAP-1 or cIAP-2. In a further embodiment the IAP can be multiple IAP types. The method may further include concurrent administration of a chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

Description of Disclosure - DETX (149):

[0187] Additional chemotherapeutic agents Chemotherapeutic agents suitable, include but are not limited to the chemotherapeutic agents described in "Modern Pharmacology with Clinical Applications", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (2004), herein incorporated by reference. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal

anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors and kinase inhibitors.

DOCUMENT-IDENTIFIER: US 20080020986 A1

TITLE: DIMERIC IAP INHIBITORS

----- KWIC -----

Description of Disclosure - DETX (114):

[0153] The method may further include the concurrent administration of another chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds

Description of Disclosure - DETX (118):

[0157] Embodiments of the invention also include a method of treating a patient with cancer by promoting apoptosis wherein administration of a therapeutically effective amount of a Smac peptidomimetic, and the Smac peptidomimetic binds to at least one TAP. In one embodiment the IAP can be XIAP. In another embodiment the IAP can be ML-IAP. In another embodiment the IAP can cIAP-1 or cIAP-2. In a further embodiment the IAP can be multiple IAP types. The method may further include concurrent administration of a chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

Description of Disclosure - DETX (127):

[0166] Additional chemotherapeutic agents Chemotherapeutic agents suitable, include but are not limited to the chemotherapeutic agents described in "Modern Pharmacology with Clinical Applications", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (2004), herein incorporated by reference. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors and kinase inhibitors.

DOCUMENT-IDENTIFIER: US 20070292401 A1

TITLE: Soft tissue repair and regeneration using stem cell products

----- KWIC -----

Description of Disclosure - DETX (142):

[0134]In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Methods of lysing cells are well-known in the art and include various means of freeze-thaw disruption, osmotic disruption, mechanical disruption, ultrasonic disruption, enzymatic disruption (e.g., hyaluronidase, dispase, proteases, and nucleases (for example, deoxyribonuclease and ribonuclease)), or chemical disruption (non-ionic detergents such as, alkylaryl polyether alcohol (TRITON.RTM. X-100), octylphenoxy polyethoxy-ethanol (Rohm and Haas, Philadelphia, Pa.), BRIJ-35, a polyethoxyethanol lauryl ether (Atlas Chemical Co., San Diego, Calif.), polysorbate 20 (TWEEN 20.RTM.), a polyethoxyethanol sorbitan monolaureate (Rohm and Haas), polyethylene lauryl ether (Rohm and Haas); and ionic detergents such as, for example, sodium dodecyl sulphate, sulfated higher aliphatic alcohols, sulfonated alkanes and sulfonated alkylarenes containing 7 to 22 carbon atoms in a branched or unbranched chain), or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Cells may also be lysed on their growth substrate. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of stem cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. In some embodiments, cellular membranes are removed from the lysate, for example by centrifugation, or ultracentrifugation, filtration, chromatograph, or sedimentation, to yield a membrane fraction and supernate fraction. The membrane fraction or the supernate may be used according to the methods of the invention. In some embodiments, the whole cell lysate or a cell fraction can be processed with molecular weight cut off filters to obtain a lysate of a particular molecular weight including, but not limited to 5,000 to 100,000 kDa. SCP filtered to obtained fractions of a defined molecular weight range can be combined with other SCP filtered fractions to obtain other specific defined molecular weight ranges. In some embodiments, cellular debris is removed by treatment with a mild detergent rinse, such as EDTA, CHAPS or a zwitterionic detergent. Cell lysates may be used in vitro or in vivo, alone or, for

example, with cells or on a substrate. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20070282016 A1

TITLE: METHODS AND COMPOSITIONS FOR USE OF ANGIOGENESIS
INHIBITORS IN THE PREVENTION AND/OR CONTROL OF EPILEPSY

----- KWIC -----

Description of Disclosure - DETX (22):

[0030] Similarly, in some embodiments, the invention comprises the selective administration of angiogenesis inhibitors that act by interacting with or blocking other steps in the biochemical effectuation of intra- or inter-cellular growth factor influence, including without limitation, VEGF influence. As two examples only, without limitation, such activity may include interacting with or disturbing the activity of integrins and/or other extracellular matrix proteins.

DOCUMENT-IDENTIFIER: US 20070281904 A1

TITLE: Chitosan-derivative compounds and methods of
controlling microbial populations

----- KWIC -----

Description of Disclosure - DETX (219):

[0184]In accordance with the present invention, additional wound healing effects, cell stimulation and molecular tracking are achieved by functionalized chitosan-co-derivative compounds including, but not limited to, iron chelating molecules and antioxidants, as shown in (16) through (19), below. In (16), below, X is (5a), (5b) or (6), above. In (17), below, X' is (8a) through (9c), above. In (18), below, X'' is (11) or (12), above. In (19), below, X''' are the natural amino acids: lysine (pka .about.10), histidine (pka .about.6), aspartic acid (asp), and glutamic acid (glu). In (16) through (19), m is related to the degree of functionalization of X, X', X'', or X''' such that the degree of functionalization is reported as a percent where $m/(1-q)100\%$. In (16) through (19), Y includes, but are not limited to, desferoxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, polypeptides and chemical cellular growth factors. Y also includes, but are not limited to, lysine (lys), histidine (his), aspartic acid (asp), glutamic acid (glu), alanine (ala), asparagine (asn), glutamine (gln), methionine (met), proline (pro), threonine (thr), serine (ser), tyrosine (tyr), and cysteine (cys). Additionally, Y is a naturally hydrophobic or weakly hydrophobic amino acids including, but not limited to, tryptophan (trp), phenylalanine (phe), valine (val), leucine (leu) and isoleucine (ile) where $X.\text{noteq}.Y$ and $X'''.\text{noteq}.Y$. Y is selected such that it is insoluble until in the lowest physiologically applicable pH. As understood by one of ordinary skill, Y is not limited to above compounds but includes others in this class of compounds. In (16) through (19), n is related the degree of functionalization of Y such that the degree of functionalization is reported as a percent where $n/(1-q)100\%$, where n is 0.001 to 0.10; p and q represent the degree of deacetylation such that q is between 0.50 and 0.01. In a preferred embodiment q is less than 0.20 and $p+q+m+n=1$.

Description of Disclosure - DETX (220):

Co-derivatives of the above defined chitosan-derivative compounds include but are not limited to desferoxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, cellular growth factors, iron chelating agents, antioxidants, indicating fluorescent markers, cell growth factors and the natural amino acids listed above;

Description of Disclosure - DETX (239):

[0199]In (29), Y includes, but are not limited to, desferoxamine

(desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, polypeptides and chemical cellular growth factors. Y also includes, but are not limited to, lysine (lys), histidine (his), aspartic acid (asp), glutamic acid (glu), alanine (ala), asparagine (asn), glutamine (gln), methionine (met), proline (pro), threonine (thr), serine (ser), tyrosine (tyr), and cysteine (cys). Additionally, Y is a naturally hydrophobic or weakly hydrophobic amino acids including, but not limited to, tryptophan (trp), phenylalanine (phe), valine (val), leucine (leu) and isoleucine (ile). As understood by one of ordinary skill, Y is not limited to above compounds but includes others in this class of compounds.

Claims Text - CLTX (21):

21. A compound as recited in claim 20, wherein said co-derivatives are selected from the group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, cellular growth factors, iron chelating agents, antioxidants, indicating fluorescent markers, cell growth factors, lysine (K), arginine (R), histidine (H), aspartic acid (D), glutamic acid (E); serine (S), threonine (T), asparagine (N), glutamine (Q), tyrosine (Y), cysteine (C); glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), methionine (M), proline (P), phenylalanine (F) and tryptophan (W).

Claims Text - CLTX (32):

32. A compound as recited in claim 31 wherein said derivative selected from the group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, cellular growth factors, iron chelating agents, antioxidants, indicating fluorescent markers, cell growth factors, lysine (K), arginine (R), histidine (H), aspartic acid (D), glutamic acid (E); serine (S), threonine (T), asparagine (N), glutamine (Q), tyrosine (Y), cysteine (C); glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), methionine (M), proline (P), phenylalanine (F) and tryptophan (W).

Claims Text - CLTX (64):

64. A method as recited in claim 63, wherein said co-derivatives are selected from the group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, cellular growth factors, iron chelating agents, antioxidants, indicating fluorescent markers, cell growth factors, lysine (K), arginine (R), histidine (H), aspartic acid (D), glutamic acid (E); serine (S), threonine (T), asparagine (N), glutamine (Q), tyrosine (Y), cysteine (C); glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), methionine (M), proline (P), phenylalanine (F) and tryptophan (W).

Claims Text - CLTX (69):

69. A method as recited in claim 68, wherein said derivatives are selected from the group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, cellular growth factors, iron chelating agents, antioxidants, indicating fluorescent markers, cell growth factors, lysine (K), arginine (R), histidine (H), aspartic acid (D), glutamic acid (E); serine (S), threonine (T), asparagine (N), glutamine (Q), tyrosine (Y), cysteine (C); glycine (G), alanine (A), valine (V), leucine (L), isoleucine (I), methionine (M), proline (P), phenylalanine (F) and tryptophan (W).

Claims Text - CLTX (97):

97. A compound as recited in claim 95, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (103):

103. A compound as recited in claim 100, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (108):

108. A compound as recited in claim 106, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (114):

114. A compound as recited in claim 111, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (136):

136. A compound as recited in claim 133, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (143):

143. A compound as recited in 139, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha

hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (149):

149. A compound as recited in claim 146 wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (158):

158. A compound as recited in claim 152, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (163):

163. A compound as recited in claim 162, wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (169):

169. A compound as recited in claim 167 wherein Y is selected from the group consisting of: ferredoxin (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, formulations of hydroxy acids, fluorescein, Texas Red, rhodamine, Prodan, and cellular growth factors.

Claims Text - CLTX (184):

184. A method as recited in claim 183, wherein said co-derivatives are selected from the group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, polypeptides and chemical cellular growth factors.

Claims Text - CLTX (190):

190. A method as recited in claim 189, wherein said derivative is selected from a group consisting of desferrioxamine (desferrioxamine), alpha hydroxy acids, poly alpha hydroxy acids, retinol, alpha lipoic acid, flavinoids, coenzyme Q, Q10, fluorescein, Texas Red, rhodamine, Prodan, polypeptides and chemical cellular growth factors.

DOCUMENT-IDENTIFIER: US 20070275365 A1

TITLE: Human Corneal Endothelial Cells and Methods of
Obtaining and Culturing Cells for Corneal Cell
Transplantation

----- KWIC -----

Claims Text - CLTX (1):

1. The method of non-enzymatic harvesting and in vitro culturing corneal epithelial cells for transplantation comprising the steps of: a) dissecting corneal endothelial cells from a tissue source; growing said corneal endothelial cells at a low density in extracellular matrix coated (ECM) culture plates for a period of time; b) passaging said cells into a secondary culture system wherein the secondary culture system is comprised of ECM coated culture plates and the addition of sufficient cellular growth factors; c) growing the corneal endothelial cells to confluency; and d) harvesting the corneal endothelial cells from the second culture system in sufficient quantities to be useful in transplantation to a subject in vivo.

Claims Text - CLTX (16):

16. A method of making HCEC cells wherein said HCEC are lacking class I HLA antigens comprising the steps of: a) dissecting human corneal epithelial cells from a neonatal source such that said cells do not express class I HLA antigens; b) growing said corneal epithelial cells at a low density in a range of about 100 to 500 cells per square millimeter in a primary culture system comprising extracellular matrix coated (ECM) culture plates for a period of time; c) passaging said cells into a secondary culture system wherein the secondary culture system is comprised of an ECM coated culture plates and the addition of sufficient cellular growth factors; d) growing said cells until the cells are confluent; and e) harvesting said cells from the second culture system in sufficient quantities to be useful in transplantation to a subject in vivo.

Claims Text - CLTX (20):

20. A method of making HCEC cells wherein said HCEC are lacking class I HLA antigens comprising the steps of: a) dissecting human corneal epithelial cells from a tissue source, growing said corneal epithelial cells at a low density in a range of about 100 to 500 cells per square millimeter in a primary culture system comprising extracellular matrix coated (ECM) culture plates for a period of time; b) passaging said cells into a secondary culture system wherein the secondary culture system is comprised of an ECM coated culture plates and the addition of sufficient cellular growth factors; c) growing said cells to confluency; d) harvesting said cells from the second culture system in sufficient quantities to be useful in transplantation to a subject in vivo; and e) transforming said cells such that the a cell line is created and said cells contain a targeted disruption in the HLA gene locus thereby inhibiting

expression of HLA antigens.

DOCUMENT-IDENTIFIER: US 20070264269 A1

TITLE: COMPOSITIONS AND METHODS FOR INHIBITING ADVERSE IMMUNE
RESPONSE IN HISTOCOMPATIBILITY-MISMATCHED
TRANSPLANTATION

----- KWIC -----

Description of Disclosure - DETX (64):

[0082] Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, enriched, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or, for example, with syngeneic or autologous live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example, needed cellular growth factors to a patient. Preferably, the lysates are not immunogenic, and more preferably they are immunologically tolerated in a broad population of syngeneic and allogeneic recipients without adverse immunological consequences or reaction. Cell lysates of the invention are useful from cells at any stage or age which have been grown under conditions for growth and expansion, for example on Growth Medium. Even senescent cells are useful for the preparation of lysate and can provide certain factors that are biologically useful. Nonviable or even dead or killed cells have utility for preparing lysates, and cellular fractions.

DOCUMENT-IDENTIFIER: US 20070264246 A1

TITLE: ENHANCED MEDICAL TREATMENTS RESULTING FROM CHEMICAL IDENTIFICATION OF CALCIUM INFLUX FACTOR, IDENTITY WITH THE FACTOR ACTIVATING PHOSPHOLIPOLYSIS AND PRECIPITATING SUDDEN DEATH DURING MYOCARDIAL INFARCTION, AND DETERMINATION OF SIMILAR ACTIVATING MECHANISMS IN MULTIPLE CELL TYPES THROUGH DISINHIBITION OF CALCIUM-INDEPENDENT PHOSPHOLIPASE A2beta

----- KWIC -----

Brief Summary Text - BSTX (4):

[0005] The function of complex living biological organisms relies on the meticulous control of cellular activity, including close regulation of cell growth, proliferation and function. The family of enzymes known as phospholipases A.sub.2 has been implicated in the control of cellular activity by catalyzing the esterolytic cleavage of fatty acids from phospholipids, thereby regulating the release of lipid second messengers, cellular growth factors, and the properties of the cellular membrane (Samuelsson et al., Annu. Rev. Biochem. 47:997-1029, 1978; Moolenaar, W. H., Curr. Opin. Cell. Biol. 7:203-10, 1995). In particular, by controlling the production of second messengers such as arachidonic acid and its biologically active eicosanoid metabolites, phospholipases A.sub.2 are involved in modulating such processes as cellular growth programs, inflammation, vascular tone and ion channel function. (Needleman et al., Annu. Rev. Biochem. 55:69-102, 1986).

DOCUMENT-IDENTIFIER: US 20070259006 A1

TITLE: Shed antigen vaccine with dendritic cells adjuvant

----- KWIC -----

Description of Disclosure - DETX (31):

[0049] Another alternative procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art. Once collected and isolated, DC or other types of antigen presenting cells are normally expended, matured and activated by incubation with a variety of cellular growth factors as described in U.S. Pat. No. 5,199,942. Other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used.

Alternatively, cytokines may be administered prior to, or concurrently with the collection of blood mononuclear cells to expend the population of DC and DC progenitor cells.

DOCUMENT-IDENTIFIER: US 20070248638 A1

TITLE: STRUCTURALLY MODIFIED ACELLULAR TISSUE ENGINEERING
SCAFFOLDS AND METHODS OF PRODUCTION

----- KWIC -----

Description of Disclosure - DETX (67):

[0063]The "extracellular matrix" or "ECM" or "interstitial structure" as used herein is any part of a tissue that is not a part of any cell. The ECM is the defining feature of connective tissue. In animals, the ECM is comprised primarily of collagen. The ECM also contains various proteins, including a wide range of cellular growth factors.

DOCUMENT-IDENTIFIER: US 20070238668 A1

TITLE: Methods of using gelsolin to treat or prevent bacterial sepsis

----- KWIC -----

Brief Summary Text - BSTX (11):

[0011] S1P is a highly active cellular growth factors that is generated enzymatically from cellular membrane precursors and secreted by activated platelets, leukocytes, epithelial cells, and some types of tumors. S1P is stored in relatively high concentrations in human platelets, which lack the enzymes responsible for its catabolism, and it is released into the blood stream upon activation by physiological stimuli, such as growth factors, cytokines, and receptor agonists and antigens. It may have a critical role in platelet aggregation and thrombosis and could aggravate cardiovascular disease. On the other hand, the relatively high concentration of the metabolite in high-density lipoproteins (HDL) may have beneficial implications for atherogenesis. For example, reportedly S1P together with other lysolipids, such as SPC and lysosulfatide, may be responsible for the beneficial clinical effects of HDL by stimulating the production of the potent antiatherogenic signaling molecule nitric oxide by the vascular endothelium. In addition, S1P functions intracellularly to regulate calcium mobilization and cell growth in response to a variety of extracellular stimuli. However, Yamamura et al., FEBS Lett. 382:193-197 (1996) dismissed the speculation that S1P could physically interact with actin-binding proteins, demonstrating that S1P was poorly active and yielded only a maximal dissociation of 10%.

DOCUMENT-IDENTIFIER: US 20070207546 A1

TITLE: BOVINE IMMUNODEFICIENCY VIRUS (BIV) BASED VECTORS

----- KWIC -----

Description of Disclosure - DETX (69):

[0085] Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

DOCUMENT-IDENTIFIER: US 20070203749 A1

TITLE: BUSINESS METHODS FOR COMPOUNDS FOR TREATMENT OF
PROLIFERATIVE DISORDERS

----- KWIC -----

Description of Disclosure - DETX (61):

[0088] In each of the above illustrative embodiments, the composition or method may further include a chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Description of Disclosure - DETX (78):

[0105] Additional chemotherapeutic agents. Chemotherapeutic agents suitable, include but are not limited to the chemotherapeutic agents described in "Modern Pharmacology with Clinical Application", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (2004), herein incorporated by reference. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors: CPT (8-Cyclopentyl-1, 3-dimethylxanthine, topoisomerase I inhibitor) and VP16 (etoposide, topoisomerase II inhibitor).

Description of Disclosure - DETX (94):

[0120] In each of the embodiments described above, the information provided and/or disseminated and data stored in the database may further include compositions, methods, or protocols for combined therapies that may include another chemotherapeutic agent. For example, a chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

DOCUMENT-IDENTIFIER: US 20070202084 A1

TITLE: Bioabsorbable implant of hyaluronic acid derivative for treatment of osteochondral and chondral defects

----- KWIC -----

Abstract Paragraph - ABTX (1):

A method for treating an osteochondral defect or a chondral defect in a subject includes implanting a composite in a site of the osteochondral or chondral defect. The composite includes a hyaluronic acid derivative; and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative. In one embodiment, carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea. In another embodiment, the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8. The composite can be used for regenerating or stimulating regeneration of meniscal tissues in a subject in need thereof.

Brief Summary Text - BSTX (5):

[0004] The present invention generally is directed to a method for treating an osteochondral defect or a chondral defect in a subject by the use of a composite that includes a hyaluronic acid derivative and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor.

Brief Summary Text - BSTX (6):

[0005] In one embodiment, the invention is directed to a method for treating an osteochondral defect or a chondral defect in a subject. The method includes implanting a composite at a site of the osteochondral or chondral defect. The composite includes a hyaluronic acid derivative; and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor. The cell, cellular growth factor or cellular differentiation factor is impregnated in, or coupled to, the hyaluronic acid derivative. The hyaluronic acid derivative includes carboxyl functionalities that are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea.

Brief Summary Text - BSTX (7):

[0006] In another embodiment, the invention is directed to a method for regenerating or promoting regeneration of cartilage and/or bone in an osteochondral defect or a chondral defect in a subject. The method includes forming a scaffold that includes a hyaluronic acid derivative and a support, wherein a portion of carboxyl functionalities of the hyaluronic acid derivative

is derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea. The method also includes the steps of impregnating in, or coupling to, the scaffold at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor; and implanting the scaffold impregnated or coupled with at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor at a site of the osteochondral defect or chondral defect, thereby providing a mechanism for the delivery of the cell, cellular growth factor or cellular differentiation factor to the site of the osteochondral or chondral defect to regenerate or promote regeneration of cartilage and bone in the osteochondral defect or chondral defect.

Description of Disclosure - DETX (4):

[0010] FIG. 3 is a cross sectional view of the composite of FIGS. 2A-2B, showing interconnected structural support that can provide cues for ingrowth of cells, cellular growth factors or cellular differentiation factors for treating an osteochondral or chondral defect.

Description of Disclosure - DETX (64):

[0069] In a preferred embodiment, the composite of the invention is an implantable composite. More preferably, the implantable composite has interconnected pores of sizes that can provide molecular cuing for the impregnated or coupled cells, cellular growth factors or cellular differentiation factors to migrate (or move) through. The interconnected pores of sizes can also provide molecular cuing for cells of a subject that are surrounding the osteochondral or chondral defect of the subject (e.g., cartilage, bone or synovium) to migrate (or move) through. In a specific example, the implantable composite is freeze-dried and has interconnected pores of sizes that can provide molecular cuing as described above.

Description of Disclosure - DETX (65):

[0070] These composites can provide structural support and molecular cuing to stimulate regeneration of cartilage and/or bone, or repair of osteochondral or chondral defects by providing a mechanism for the delivery of, for example, cells to a site of osteochondral or chondral defects, or a site in need of regeneration of cartilage and/or bone. For example, the composite of the invention can provide the cells, cellular growth factors or cellular differentiation factors that are impregnated in, or coupled to, the composite to regenerate articular cartilage and/or bone in the osteochondral or chondral defect, or repair the osteochondral or chondral defect. The biocompatible, biodegradable support and the hyaluronic acid derivative will be absorbed by the body (e.g., by the regenerated tissues), while the repair or regeneration takes place. After the biodegradation of the composite, for example, the regenerated articular cartilage can have physical characteristics of natural articular cartilage and assume its normal function.

Description of Disclosure - DETX (69):

[0074] A composite of the invention includes at least one member of the group consisting of a cell, a cellular growth factor and a cellular

differentiation factor, which is impregnated in, or coupled to, the HA derivative, or the composite that includes the HA derivative, and biocompatible and biodegradable support. Suitable examples of the cell, cellular growth factor and cellular differentiation factor include mesenchymal stem cells from various tissue sources (e.g., cartilage, periosteum, synovium, bone marrow, fat, etc.), fibrochondrocytes, osteochondrocytes, chondrocytes, TGF.β, supergene family members, such as BMPs, IGF, PDGF, GDFs, CDMPs and GFG, and tissue growth hormones. In addition, genes encoding for these proteins, as well as synthetic peptide analogues of these proteins can be contemplated. In a preferred embodiment, the composite include at least one member selected from the group consisting of cartilage chondrocytes, osteochondrocytes and mesenchymal stem cells. In another preferred embodiment, the composite includes both a cell, and a cellular growth or differentiation factor. The cellular growth or differentiation factor can provide molecular cuing for the cell to produce cartilage or bone tissue, or provide signals for the cell to differentiate down the chondrogenic or osteogenic lineage.

Description of Disclosure - DETX (70):

[0075] Typically, the cells, cellular growth factor and/or cellular differentiation factors are harvested from various sources and impregnated in, or coupled to, the HA derivative or the HA derivative and biocompatible support, by methods known in the art. For example, autologous cells (e.g., chondrocytes or marrow-derived pluripotent stem cells) can be harvested, optionally expanded in culture, and loaded onto a composite of the invention by conventional cell seeding methods. The cell-loaded composite may be further cultured prior to implantation. Additionally, cells, cellular growth factors and cellular differentiation factors can be loaded prior to implantation by various means. These cells or factors can be loaded before (e.g., suspension, covalent linking, etc) or after (e.g., soak-loading, surface immobilization, etc.) manufacture of the composite.

Claims Text - CLTX (1):

1. A method for treating an osteochondral defect or a chondral defect in a subject, comprising implanting a composite in a site of the osteochondral or chondral defect, the composite including: a) a hyaluronic acid derivative, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (15):

15. A method for regenerating or promoting regeneration of cartilage and/or bone in an osteochondral or chondral defect in a subject, comprising: a) forming a scaffold that includes a hyaluronic acid derivative and a support, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; b) impregnating in, or coupling to, the scaffold at least one member of the group consisting of a cell, and a cellular

growth and differentiation factor in the scaffold; and c) implanting the scaffold that is impregnated or coupled with said at least one member of the group consisting of a cell, and a cellular growth and differentiation factor at a site of the osteochondral or chondral defect of the subject, thereby providing a mechanism for delivery of the cell, cellular growth factor or cellular differentiation factor to the site of the osteochondral or chondral defect to regenerate or promote regeneration of cartilage and bone in the osteochondral or chondral defect.

Claims Text - CLTX (16):

16. The method of claim 15, wherein the cell, cellular growth factor and cellular differentiation factor include at least one member selected from the group consisting of mesenchymal stem cells, fibrochondrocytes, osteochondrocytes, chondrocytes, TGF.beta. supergene family members, and hormones that stimulate tissue growth.

Claims Text - CLTX (22):

22. The method of claim 15, wherein the scaffold has interconnected pores of sizes that can provide molecular cuing for the impregnated or coupled cell to migrate through, or a path for migration of the impregnated or coupled cellular growth factor or cellular differentiation factor.

DOCUMENT-IDENTIFIER: US 20070197428 A1

TITLE: Novel indications of mannan-binding lectin (MBL) in the treatment of immuno-compromised individuals

----- KWIC -----

Description of Disclosure - DETX (28):

[0110] Other biologic and immunomodulating agents have been used in treatment of patients with neutropenia and fever. Intravenous immunoglobulin has no benefit in preventing fever or infection in patients with neutropenia, but may have a moderate effect in patients with antibody deficiencies. Interferon gamma may add a benefit to patients with some neutrophil deficiencies, but this is not finally proven. Cellular growth factors (granulocyte and granulocyte-macrophage colony-stimulating factor) may shorten the duration of neutropenia and thus the need for antibiotics.

DOCUMENT-IDENTIFIER: US 20070196342 A1

TITLE: Meniscal implant of hyaluronic acid derivatives for treatment of meniscal defects

----- KWIC -----

Abstract Paragraph - ABTX (1):

A composite for treating an articular defect includes a hyaluronic acid derivative; and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative. In one embodiment, carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea. In another embodiment, the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8. The composite can be used for regenerating or stimulating regeneration of meniscal tissues in a subject in need thereof.

Brief Summary Text - BSTX (7):

[0006] In one aspect, the invention is directed to a composite for treating an articular defect, such as a meniscal defect. The composite includes a hyaluronic acid derivative, and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor. The cell, cellular growth factor or cellular differentiation factor is impregnated in, or coupled to, the hyaluronic acid derivative. In one embodiment, carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea. In another embodiment, the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8.

Brief Summary Text - BSTX (8):

[0007] In another aspect, the invention is directed to a meniscal augmentation device having a shape of a meniscal defect in meniscus. The meniscal augmentation device includes a hyaluronic acid derivative, and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative. Preferably, the cell, cellular growth factor and cellular differentiation factor include at least one member selected from the group consisting of mesenchymal stem cells, periosteal cells, synoviocytes, fibrochondrocytes, osteochondrocytes, chondrocytes, TGF β supergene family members, tissue growth hormones, encoding genes thereof, and synthetic peptide analogues thereof. The hyaluronic acid derivative is as described above for the composite for treating an articular defect.

Brief Summary Text - BSTX (9):

[0008] The present invention also provides a method of regenerating or stimulating regeneration of meniscus tissues in a subject. The method includes implanting a composite at a site of the meniscus defect. The composite includes a hyaluronic acid derivative, and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative. The hyaluronic acid derivative is as described above for the composite for treating an articular defect.

Description of Disclosure - DETX (4):

[0012] FIG. 3 is a cross sectional view of the composite of FIGS. 2A-2B, showing interconnected structural support that can provide cues for ingrowth of cells, cellular growth factors or cellular differentiation factors for tissue regeneration.

Description of Disclosure - DETX (64):

[0071] In a preferred embodiment, the composite of the invention is an implantable composite. More preferably, the implantable composite has interconnected pores of sizes that can provide molecular cuing for the impregnated or coupled cells, or a path for migration of the impregnated or coupled cellular growth factors or cellular differentiation factors. The interconnected pores of sizes can also provide molecular cuing for cells of a subject that are surrounding the treatment site (e.g., cartilage, bone or synovium) to migrate (or move) through. In a specific example, the implantable composite is freeze-dried and has interconnected pores of sizes that can provide molecular cuing for the impregnated or coupled cell to migrate through, or a path for migration of the impregnated or coupled cellular growth factor or cellular differentiation factor. The implantable composite can also provide molecular cuing for cells of the subject surrounding the treatment site to migrate through.

Description of Disclosure - DETX (65):

[0072] These composites can provide structural support and molecular cuing to stimulate regeneration of meniscal tissues by providing a mechanism for the delivery of, for example, cells to regenerate or promote regeneration of articular tissues, such as meniscus tissues. For example, the cells, cellular growth factors or cellular differentiation factors impregnated in or coupled to the hyaluronic acid derivatives can migrate into an articular defect site and regenerate articular tissues or repair the articular defect. The biocompatible, biodegradable support and the hyaluronic acid derivative will be absorbed by the body (e.g., by the regenerated tissues), while the tissue regeneration and remodeling takes place. After the biodegradation of the composite, the regenerated articular tissues, such as meniscus tissues, have the physical characteristics of natural articular tissues and assume their normal function.

Description of Disclosure - DETX (69):

[0076] The rate at which the cellular growth factor or cellular growth

differentiation factor in the composites of the invention is released can also be controlled by varying the physical characteristics of the composite, such as porosity and interconnectivity, or varying the HA crosslink density. Typically, the retention of the cellular growth factor or cellular differentiation factor will range from about 1 day to 6 months, and preferably in the 2-4 weeks range.

Description of Disclosure - DETX (70):

[0077] A composite of the invention includes at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor. The cell, cellular growth factor or cellular differentiation factor is impregnated in, or coupled to, the HA derivative or the HA derivative and biocompatible, biodegradable support. Suitable examples of the cell, cellular growth factor and cellular differentiation factor include mesenchymal stem cells from various tissue sources (e.g., cartilage, periosteum, synovium, bone marrow, fat, etc.), fibrochondrocytes, osteochondrocytes, chondrocytes, TGF.β supergene family members, such as BMPs, IGF, PDGF, GDFs, CDMPs and GFG, and tissue growth hormones. In addition, genes encoding for these proteins, as well as synthetic peptide analogues of these proteins can be contemplated. In a preferred embodiment, the composite include at least one member selected from the group consisting of mesenchymal stem cells, fibrochondrocytes, osteochondrocytes and chondrocytes. In another preferred embodiment, the composite includes both a cell and a cellular growth factor or cellular differentiation factor. The cellular growth and differentiation factors can provide molecular cuing for the cell, for example, to produce a meniscal tissue, or provide signals for the cell to differentiate down the meniscal tissue.

Description of Disclosure - DETX (71):

[0078] Typically, the cells, cellular growth factors and cellular differentiation factors are harvested or obtained from various sources and impregnated in, or coupled to, the HA derivative by methods known in the art. For example, autologous cells (e.g., chondrocytes or marrow-derived pluripotent stem cells) can be harvested, optionally expanded in culture, and loaded on to the meniscal implants by conventional cell seeding methods. The cell-loaded implants may be further cultured prior to implantation. Additionally, cellular growth factors or cellular differentiation factors can be loaded prior to implantation by various means. These factors can be loaded before (e.g., suspension, covalent linking, etc) or after (e.g., soak-loading, surface immobilization, etc.) manufacture of the implant.

Description of Disclosure - DETX (72):

[0079] The composite of the invention described above can be used for the meniscal augmentation device having a shape of a meniscal defect in the meniscus. The meniscal augmentation device includes at least one member of the group consisting of fibrochondrocytes, mesenchymal stem cells and cellular growth and differentiation factors, which is impregnated in, or coupled to, a biocompatible, biodegradable support and an HA derivative, as described above. The features, including preferred parameters, of the biocompatible,

biodegradable support and HA derivative are as described above. Preferably, the cell, cellular growth factor or cellular differentiation factor includes at least one member selected from the group consisting of fibrochondrocytes, osteochondrocytes, periosteal cell, synoviocytes, chondrocytes, mesenchymal stem cells, cellular growth and differentiation factors, gene encoding for these proteins and synthetic peptide analogues of these proteins.

Description of Disclosure - DETX (100):

[0098] Sponges 1 and 2 of Examples 4 and 5, the composite made by method of Example 6 and sponges that can be made by the methods described in Examples 7-9, respectively, can provide scaffolds adapted for the loading and ingrowth of cells (such as meniscal fibrochondrocytes), cellular growth factors and/or cellular differentiation factors. FIG. 3 shows a cross sectional SEM image of Sponge 2 showing interconnected pores that can provide cues for the loaded cells to move or migrate and multiply, or for the loaded cellular growth or differentiation factors to move and migrate and exert local activity, to thereby treating meniscal defects.

Claims Text - CLTX (1):

1. A composite for treating an articular defect, comprising: a) a hyaluronic acid derivative, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (7):

7. The composite of claim 6, wherein the composite has interconnected pores of sizes that can provide molecular cuing and scaffolding for the impregnated or coupled cell, or path for migration of the cellular growth factor or cellular differentiation factor.

Claims Text - CLTX (18):

18. A meniscal augmentation device having a shape of a meniscal defect in meniscus, comprising: a) a hyaluronic acid derivative, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (19):

19. The meniscal augmentation device of claim 18, wherein said at least one cell, cellular growth factor or cellular differentiation factor includes at least one member selected from the group consisting of mesenchymal stem cells, periosteal cells, synoviocytes, fibrochondrocytes, osteochondrocytes, chondrocytes, TGF.β. supergene family members, tissue growth hormones, encoding genes thereof, and synthetic peptide analogues thereof.

Claims Text - CLTX (24):

24. The meniscal augmentation device of claim 18, wherein the composite has interconnected pores of sizes that can provide molecular cuing for the impregnated or coupled cell, or a path for migration of the cellular growth factor or cellular differentiation factor.

Claims Text - CLTX (31):

31. A method of regenerating or stimulating regeneration of meniscus tissues in a subject, comprising implanting a composite at a meniscus defect site, the composite including: a) a hyaluronic acid derivative, wherein carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (38):

38. The method of claim 31, wherein the composite has interconnected pores of sizes that can provide molecular cuing and scaffolding for the impregnated or coupled cell to migrate through, or a path for migration of the impregnated or coupled cellular growth factor or cellular differentiation factor.

Claims Text - CLTX (45):

45. A composite for treating an articular defect, comprising: a) a hyaluronic acid derivative, wherein the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (46):

46. A meniscal augmentation device having a shape of a meniscal defect in meniscus, comprising: a) a hyaluronic acid derivative, wherein the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

Claims Text - CLTX (47):

47. A method of regenerating or stimulating regeneration of meniscus tissues in a subject, comprising implanting a composite at a treatment site of the meniscus defect, the composite including: a) a hyaluronic acid derivative, wherein the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8; and b) at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation

factor, which is impregnated in, or coupled to, the hyaluronic acid derivative.

DOCUMENT-IDENTIFIER: US 20070178435 A1

TITLE: COMPOSITION FOR MAINTAINING ORGAN AND CELL VIABILITY

----- KWIC -----

Brief Summary Text - BSTX (12):

[0010] In one aspect of the invention there is provided a two-phase composition for maintaining cellular viability. The composition includes a first phase comprising a base nutritive medium; and a second phase comprising nanoparticles having an outer lipophilic coating and an inner hydrophilic core, wherein [0011] a) the first phase comprises physiologically compatible concentrations/amounts of water soluble or dispersible nutrients, and physiological salts; [0012] b) the nanoparticles of the second phase comprise one or more of the following: lipids, fatty acids, sterols, free fatty acids, optional cellular growth factors; and [0013] c) the two-phase composition has an osmolality of at least about 300 mOsM/kg.

Description of Disclosure - DETX (28):

[0042] In another preferred embodiment, the second phase also includes hydrophilic supportive endocrine factors such as hydrocortisone, thyroxine or its derivatives, and the like. Further supportive components can include, for example, cellular growth factors, e.g., epithelial and endothelial growth factors, including physiologically compatible amounts of vascular endothelial growth factor, platelet derived endothelial growth factor, epithelial growth factor, hepatocyte growth factor, platelet derived endothelial growth factor, and the like. Optionally, other factors contemplated to be included in the second phase include intercellular messengers such as prostaglandins, e.g., prostaglandin E1. Preferably, physiologically compatible surfactants and detergents are also included, e.g., one or more water-soluble surfactants, preferably an amphiphilic block copolymer with a molecular weight of several thousand Daltons, such as a polypropyleneoxide-polyethyleneoxide block copolymer surfactant (e.g., Pluronic F-68; from BASF) and/or nonionic surfactants. Suitable nonionic surfactants include, e.g., polyoxyethylene derivatives of sorbitol esters, e.g., polyoxyethylene sorbitan monooleate surfactants that are commercially available as TWEEN.RTM. (Atlas Chemical Co.). TWEEN 80.RTM. is particularly preferred. The core portion of the two-phase compositions of the invention preferably does not include a pharmaceutically significant quantity of a phosphatidic acid or sugar, or a lysophosphatidic acid or sugar.

Claims Text - CLTX (6):

6. The method of claim 1, wherein the composition further comprises cellular growth factors.

Claims Text - CLTX (7):

7. The method of claim 6, wherein said cellular growth factors are selected

from the group consisting of epithelial and endothelial growth factors, vascular endothelial growth factors, platelet derived endothelial growth factors, epithelial growth factors, hepatocyte growth factors, and mixtures thereof

DOCUMENT-IDENTIFIER: US 20070172486 A1

TITLE: Expression Of Cyclin G1 In Tumors

----- KWIC -----

Description of Disclosure - DETX (92):

[0098] Polynucleotides encoding therapeutic agents which may be contained in the retroviral plasmid vector include, but are not limited to, polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma., genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multi-drug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

DOCUMENT-IDENTIFIER: US 20070170071 A1

TITLE: Material and device properties modification by electrochemical charge injection in the absence of contacting electrolyte for either local spatial or final states

----- KWIC -----

Description of Disclosure - DETX (73):

[0088] Biocompatibility of the surfaces of devices implanted in the body is improved in some invention embodiments by overcoating these surfaces with a porous material having a high gravimetric surface area, such as glassy carbon. Using the device with the over coated porous material as an electrode in an electrochemical cell, charge is injected predominantly non-faradaically in the porous coating. The type (holes or electron) and degree of charge injection, as well as the nature of the counter ion to the injected charge, can affect biocompatibility. The injected ions can be either those of the original electrolyte or those that substitute for the original ions during subsequent processes, such as by immersion of the charge injected device into a solution containing the replacement ions. As an alternative to this charge injection into porous coatings that are preformed on the article to be implanted, such as a pacemaker or an artificial heart, the electronic charge injection can be in a powder (such as nanofibers) that are first charge injected and then used to overcoat the article. The sign of electronic charge injection is typically positive, although negative electronic charge injection can also be used (with some decrease in the lifetime on injected charge in the body). The counter ions for the electronically injected charge can include various inorganic, organic, and biochemically derived species. Examples are Na.sup.+ , Cl.sup.- , proteins (especially enzymes that are cellular growth factors), antibiotics, DNA, and RNA. Nanofibers (particularly nanofibers configured as porous sheets and macrofibers) are particularly useful as substrate materials for the growth of tissue either in culture media or in animal or human bodies. Considerations on the choice of counter ions and the sign of charge injection are similar to those above-recited for surface coatings for implanted devices.

DOCUMENT-IDENTIFIER: US 20070160976 A1

TITLE: Novel cellular function regulating agent produced by a
chondrocyte capable of hypertrophication

----- KWIC -----

Description of Disclosure - DETX (146):

[0269] "Growth factor" or "cellular growth factor" used herein interchangeably refers to a substance which enhances or controls the induction of the growth and differentiation of cells. Growth factor is also a proliferation or development factor. In cell culture or tissue culture, growth factors can be added to the medium and substituted for the function of macromolecules in the serum. It is proved that, in addition to cell growth, many growth factors function as factors that regulate differentiation.

DOCUMENT-IDENTIFIER: US 20070160588 A1

TITLE: Treatment Of Peripheral Vascular Disease Using
Postpartum-Derived Cells

----- KWIC -----

Description of Disclosure - DETX (64):

[0082] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20070149475 A1

TITLE: AUGMENTATION OF WOUND HEALING BY eIF-4E mRNA AND EGF mRNA

----- KWIC -----

Description of Disclosure - DETX (9):

[0035] Specifically, the present invention also provides a method to augment wound healing by intracellular delivery of mRNA encoding translation initiation factor eIF4E in combination with mRNA encoding cellular growth factors such as EGF. Biolistic treatment of incisional wounds with eIF4E mRNA and EGF mRNA augments wound healing in normal animals to a greater extent than animals treated with eIF4E mRNA or EGF alone. This synergistic effect was not predicted. In fact, based upon the prior art, it was unexpected that mRNA would have a predictable effect in vivo.

DOCUMENT-IDENTIFIER: US 20070148246 A1

TITLE: Nucleic Acid-Based Matrixes

----- KWIC -----

Description of Disclosure - DETX (37):

[0065] As used herein, the terms "biologically active agent" or "bioactive agent" are used interchangeably and include but are not limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, peptide, peptide mimetic, protein (e.g. antibody, angiogenic, anti-angiogenic and cellular growth factors), an antigen or immunogen, liposome, small interfering RNA, or a polynucleotide (e.g. vector, virus, viral vector, or anti-sense), therapeutic agents, organic or inorganic molecules can include a homogenous or heterogeneous mixture of compounds, including pharmaceuticals, radioisotopes, crude or purified plant extracts, and/or a cell, entities that alter, inhibit, activate, or otherwise affect biological or biochemical events, including classes of molecules (e.g., proteins, amino acids, peptides, polynucleotides, nucleotides, carbohydrates, sugars, lipids, nucleoproteins, glycoproteins, lipoproteins, steroids, growth factors, chemoattractants, etc.) that are commonly found in cells and tissues, whether the molecules themselves are naturally-occurring or artificially created (e.g., by synthetic or recombinant methods). Such agents may be naturally derived or synthetic.

DOCUMENT-IDENTIFIER: US 20070142292 A1

TITLE: COMPOSITION OF LACTOFERRIN RELATED PEPTIDES AND USES THEREOF

----- KWIC -----

Description of Disclosure - DETX (210):

[0236] A wound is also further defined as a chronic wound. Examples of chronic wounds or chronic ulcers include, but are not limited to diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Yet further, chronic wounds can also include infected wounds. Chronic wounds are wounds that do not repair or do so extremely slowly, and show partial or total lack of structural organization and functional coordination with normal tissue. Chronic wounds or chronic ulcers can be broadly classified into three major types: diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Diabetic ulcers often occur on a foot. Chronic diabetic state and poor glucose control results in poor peripheral circulation and microcirculation due to progressive arteriosclerosis; neuropathic changes that result in an insensate extremity prone to trauma; and intrinsic defects in the wound healing process that may include reduced abundance and response to cellular growth factors. In the case of venous ulcers, venous hypertension causes disturbed microcirculation and pathological changes of the capillaries, elevated persistent levels of pro-inflammatory cytokines and proteases. Fibroblast senesce and respond less to growth factors, which distribute unfavorably. Proteolytic enzymes and their inhibitors are imbalanced. Pressure ulcers occur when skin is under pressure without movement to allow blood flow for 8-12 hours.

DOCUMENT-IDENTIFIER: US 20070117177 A1

TITLE: Nucleic Acid-Based Matrixes for Protein Production

----- KWIC -----

Description of Disclosure - DETX (37):

[0065] As used herein, the terms "biologically active agent" or "bioactive agent" are used interchangeably and include but are not limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, peptide, peptide mimetic, protein (e.g. antibody, angiogenic, anti-angiogenic and cellular growth factors), an antigen or immunogen, liposome, small interfering RNA, or a polynucleotide (e.g. vector, virus, viral vector, or anti-sense), therapeutic agents, organic or inorganic molecules can include a homogenous or heterogeneous mixture of compounds, including pharmaceuticals, radioisotopes, crude or purified plant extracts, and/or a cell, entities that alter, inhibit, activate, or otherwise affect biological or biochemical events, including classes of molecules (e.g., proteins, amino acids, peptides, polynucleotides, nucleotides, carbohydrates, sugars, lipids, nucleoproteins, glycoproteins, lipoproteins, steroids, growth factors, chemoattractants, etc.) that are commonly found in cells and tissues, whether the molecules themselves are naturally-occurring or artificially created (e.g., by synthetic or recombinant methods). Such agents may be naturally derived or synthetic.

DOCUMENT-IDENTIFIER: US 20070108068 A1

TITLE: Material and device properties modification by electrochemical charge injection in the absence of contacting electrolyte for either local spatial or final states

----- KWIC -----

Description of Disclosure - DETX (73):

[0088] Biocompatibility of the surfaces of devices implanted in the body is improved in some invention embodiments by overcoating these surfaces with a porous material having a high gravimetric surface area, such as glassy carbon. Using the device with the over coated porous material as an electrode in an electrochemical cell, charge is injected predominantly non-faradaically in the porous coating. The type (holes or electron) and degree of charge injection, as well as the nature of the counter ion to the injected charge, can affect biocompatibility. The injected ions can be either those of the original electrolyte or those that substitute for the original ions during subsequent processes, such as by immersion of the charge injected device into a solution containing the replacement ions. As an alternative to this charge injection into porous coatings that are preformed on the article to be implanted, such as a pacemaker or an artificial heart, the electronic charge injection can be in a powder (such as nanofibers) that are first charge injected and then used to overcoat the article. The sign of electronic charge injection is typically positive, although negative electronic charge injection can also be used (with some decrease in the lifetime on injected charge in the body). The counter ions for the electronically injected charge can include various inorganic, organic, and biochemically derived species. Examples are Na.sup.+ , Cl.sup.- , proteins (especially enzymes that are cellular growth factors), antibiotics, DNA, and RNA. Nanofibers (particularly nanofibers configured as porous sheets and macrofibers) are particularly useful as substrate materials for the growth of tissue either in culture media or in animal or human bodies. Considerations on the choice of counter ions and the sign of charge injection are similar to those above-recited for surface coatings for implanted devices.

DOCUMENT-IDENTIFIER: US 20070104752 A1

TITLE: Aneurysm embolization material and device

----- KWIC -----

Claims Text - CLTX (24):

24. The biocompatible string, sleeve or coil of claim 19 and further comprising cellular growth factors or genes, or gene products or drugs in and on the annular main body.

DOCUMENT-IDENTIFIER: US 20070093422 A1

TITLE: Drug comprising synthetic peptide analogs for the treatment of cancer

----- KWIC -----

Brief Summary Text - BSTX (11):

[0009] The receptor tyrosine kinases (RTK) are transactivated by G protein coupled receptors (GPCR). Platelet derived growth factor (PDGF), epidermal growth factor (EGF) and insulin like growth factor 1 (IGF1) are tyrosine phosphorylated subsequent to GPCR activation. The phosphorylated growth factors in turn recruit multiple accessory proteins to activate the mitogen activated protein kinases (MAPK). Human adenocarcinomas have increased constitutive MAPK activity (Ostrowski et al, Br. J Cancer Vol 78, 1301-1306, 1997), and the blockade of this protein kinase suppresses tumour growth in vitro and in vivo (Sebolt-Leopold et al, Nature Medicine, Vol 5, 810-816, 1999). The MAP Kinase pathway is a crucial convergence point for many cytoplasmic signaling networks MAP kinases form a family of Ser/Thr kinases, which can be activated by cellular growth factors. MAP Kinase lies downstream of the Ras-Raf oncogenic pathway and its activation leads to phosphorylation of nuclear transcription factors resulting in cell proliferation (Ostrowski et al., Br.J Cancer Vol 78, 1301-1306, 1997).

DOCUMENT-IDENTIFIER: US 20070092866 A1

TITLE: Avian adenoassociated virus and uses thereof

----- KWIC -----

Description of Disclosure - DETX (26):

[0063] Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV vector can include, but are not limited to the following: nucleic acids encoding secretory and non-secretory proteins, nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; interleukins, such as IL-1, IL-1.beta., and ILs-2 through -14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; anti-HIV decoy tar elements; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Another target cell is the lung airway cell, which can be used to administer nucleic acids, such as those coding for the cystic fibrosis transmembrane receptor, which could provide a gene therapeutic treatment for cystic fibrosis. Other target cells include muscle cells where useful nucleic acids, such as those encoding cytokines and growth factors, can be transduced and the protein the nucleic acid encodes can be expressed and secreted to exert its effects on other cells, tissues and organs, such as the liver. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

DOCUMENT-IDENTIFIER: US 20070088081 A1

TITLE: Polyamine conjugates as selective NMDA inhibitors and
anti-cancer drugs

----- KWIC -----

Brief Summary Text - BSTX (6):

[0005] Polyamines are naturally occurring amines, which form polycations in vivo. These stabilize DNA architectures and are cellular growth factors. All cells contain some form of the native polyamines: putrescine, spermidine or spermine. Rapidly dividing cells (such as cancer cells) require large amounts of polyamines, and cells can either biosynthesize or import these essential growth factors. Many tumor cell lines have been shown to have very high levels of polyamines and an active polyamine transporter.

DOCUMENT-IDENTIFIER: US 20070087982 A1

TITLE: Methods of treatment and diagnosis using modulators of virus-induced cellular gene sequences

----- KWIC -----

Description of Disclosure - DETX (251):

[0293] HIV-infected THP-1 cells. HIV-infected THP-1 cells were used as an in vitro model for examining cellular gene expression during the HIV replication cycle. The HIV-1 89.6 was initially grown in PBMC, and concentrated using Amicon membranes prior to use for infection of THP-1 cells. Briefly, as the goal of the present studies was to profile cellular gene expression over the course of a complete viral replication cycle, the protocol called for synchronous infection of the majority of cells in culture, with multiple samplings over the first 48 hours post-infection (PI). Since the number of target cells required to yield sufficient RNA for gene profiling at multiple times PI is high ($>10^{10}$), synchronous infection of such cell numbers requires high titer virus stocks. However, virus titers derived from PBMC supernatants are typically only in the region of 1×10^5 to 1×10^6 pfu/ml. Additionally, such supernatants may also contain cellular growth factors with the capacity to influence gene expression independent of virus-induced effects.

DOCUMENT-IDENTIFIER: US 20070087047 A1

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (4):

[0003] A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments for use in active immunity, cytokines and cellular growth factors for stimulating immunological inflammatory responses, hormones, and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, N. V., et al., Proc. Natl. Acad. Sci. USA 84:1487-1491 (1987); Philips, M. L., et al., Science 250:1130-1132 (1990); Waldmann, T. A., Annu. Rev. Immunol. 10:675-704 (1992)).

Brief Summary Text - BSTX (14):

[0012] (c) a cytokine or a cellular growth factor, for use in stimulating an immune response in the subject;

Claims Text - CLTX (2):

2. The composition of claim 1 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (8):

8. The composition of claim 7 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

DOCUMENT-IDENTIFIER: US 20070083187 A1

TITLE: APPARATUS AND METHODS FOR DELIVERING STEM CELLS AND
OTHER AGENTS INTO CARDIAC TISSUE

----- KWIC -----

Description of Disclosure - DETX (48):

[0062] The source of fluid 40 may include one or more agents, e.g., dissolved, suspended, or otherwise carried by the fluid. For example, the one or more agents may include stem cells, genes, proteins, small molecules, cellular and other growth factors, and the like. The fluid may be any liquid or gas capable of sufficiently inflating the sheath 30 and/or pressurizing the target vessel, e.g., water, saline, carbon dioxide, and the like.

Alternatively, a separate source of agent(s) (not shown) may be provided that is coupled to a port (also not shown) on the handle 50. The source of agent(s) may be independently deliverable through the apparatus 8, e.g., through the same lumen as or a separate from the source of fluid 40. Alternatively, the source of fluid may be capable of adding one or more agents to the fluid after initially delivering fluid without such agent(s).

Claims Text - CLTX (23):

23. The method of claim 21, wherein the one or more agents comprise cellular growth factors.

DOCUMENT-IDENTIFIER: US 20070072291 A1

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Brief Summary Text - BSTX (11):

[0010] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) isolating the monocytes from human blood; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (12):

[0011] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) providing human monocytes; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (17):

[0016] The present invention includes and provides a dedifferentiated, programmable stem cell of human monocytic origin manufactured by a process comprising (a) isolating monocytes from human blood; (b) propagating monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

DOCUMENT-IDENTIFIER: US 20070072282 A1

TITLE: Bovine adeno-associated viral (baav) vector and uses thereof

----- KWIC -----

Description of Disclosure - DETX (29):

[0087] Examples of exogenous nucleic acids which can be administered to a cell or subject as part of the present BAAV vector can include, but are not limited to the following: nucleic acids encoding secretory and nonsecretory proteins, nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma., interleukins, such as IL-1, IL-1.beta., and ILs -2 through -14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; omithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; anti-HIV decoy tar elements; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Another target cell is the lung airway cell, which can be used to administer nucleic acids, such as those coding for the cystic fibrosis transmembrane receptor, which could provide a gene therapeutic treatment for cystic fibrosis. Other target cells include muscle cells where useful nucleic acids, such as those encoding cytokines and growth factors, can be transduced and the protein the nucleic acid encodes can be expressed and secreted to exert its effects on other cells, tissues and organs, such as the liver. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Description of Disclosure - DETX (136):

[0229] Provided are recombinant vectors based on BAAV. Such vectors may be useful for transducing erythroid progenitor cells or cells resistant to transduction by other serotypes of AAV. These vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some examples of this type of treatment

include, but are not limited to, the introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

DOCUMENT-IDENTIFIER: US 20070060651 A1

TITLE: Compositions and methods for improving functional
vascular cellular survival integrity and reducing
apoptosis in ischemia

----- KWIC -----

Brief Summary Text - BSTX (15):

[0013] In certain embodiments, the composition is a pet food composition, dietary supplement, or a food product formulated for human consumption. In various embodiments, the LCPUFA include at least one of arachidonic acid, eicosapentaenoic acid, docosapentaenoic acid, and docosahexaenoic acid, and the NORC include at least one of L-arginine and derivatives thereof. The compositions may comprise additional ingredients. For example, one or more antioxidants, vitamins, e.g. B-vitamins, cellular growth factors, anti-inflammatory agents, and any combination thereof may also be included.

DOCUMENT-IDENTIFIER: US 20070053872 A1

TITLE: TREATMENT OF WOUNDS USING IL-17B

----- KWIC -----

Description of Disclosure - DETX (19):

[0040] SCF is a novel cellular growth factor that stimulates the growth of early hematopoietic progenitor cells, neural stem cells, and primordial germ stem cells (PCT/US90/05548, filed Sep. 28, 1990). SCF exhibits potent synergistic activities in conjunction with colony stimulating factors, resulting in increased numbers of colonies and colonies of greater size (Martin et al., (1990) Cell, vol. 63: 203-11). Thus, administration of SCF to mammals in pharmacologic doses, alone or in combination with other colony stimulating factors or other hematopoietic growth factors, may lead to the improvement of damaged cells in a number of divergent organ systems.

DOCUMENT-IDENTIFIER: US 20070042428 A1

TITLE: TREATMENT OF PROLIFERATIVE DISORDERS

----- KWIC -----

Description of Disclosure - DETX (66):

[0083] In each of the above illustrative embodiments, the composition or method may further include a chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-estrogenic analogs.

Description of Disclosure - DETX (83):

[0100] Additional chemotherapeutic agents. Chemotherapeutic agents suitable, include but are not limited to the chemotherapeutic agents described in "Modern Pharmacology with Clinical Applications", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (200), herein incorporated by reference. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors: CPT (8-Cyclopentyl-1,3-dimethylxanthine, topoisomerase I inhibitor) and VP16 (etoposide, topoisomerase II inhibitor).

DOCUMENT-IDENTIFIER: US 20070042338 A1

TITLE: Method for storing tumor cells

----- KWIC -----

Brief Summary Text - BSTX (46):

[0046] In a general aspect the present invention provides the use of a two-phase liquid composition for storing and stabilizing tumor tissue, wherein the first phase of the liquid composition comprises a base nutritive medium and the second phase comprises liposomes. The base nutritive medium comprises physiologically compatible concentrations of water-soluble or dispersible nutrients and physiological salts, for example amino acids, salts, vitamins, nucleotides, carbohydrates and anti-oxidants. The liposomes of the second phase are nanoparticles which comprise sterols, preferably cholesterol, and, optionally, fatty acids and cellular growth factors. The supposed structure of the liposomes comprises an outer lipophilic coating and an inner hydrophilic core.

Brief Summary Text - BSTX (58):

[0058] In another preferred embodiment, the second phase includes hydrophilic supportive endocrine factors such as hydrocortisone, thyroxine, or its derivatives, and the like. Further supportive components include cellular growth factors, e.g. epithelial and endothelial growth factors, including physiologically compatible amounts of vascular endothelial growth factor, platelet derived endothelial growth factor, epithelial growth factor, hepatocyte growth factor, platelet derived-endothelial growth factor, and the like. Optionally, other factors contemplated to be included in the second phase include inter-cellular messengers such as prostaglandins, e.g. prostaglandin E1. Preferably, physiologically compatible surfactants and detergents are also included, e.g. one or more water-soluble surfactant, preferably an amphiphilic block copolymer with a molecular weight of several thousand Daltons, such as a polypropyleneoxide-polyethyleneoxide block copolymer surfactant (e.g. Pluronic F-68; from BASF) and/or nonionic surfactants. Suitable nonionic surfactants include, e.g. polyoxyethylene derivatives of sorbitol esters, e.g. polyoxyethylene sorbitan monooleate surfactants that are commercially available as TWEEN.RTM. (Atlas Chemical Co.). TWEEN 80.RTM. is particularly preferred.

Claims Text - CLTX (31):

60. A method of preparing a composition for storing cells, said method comprising: preparing a base nutritive medium comprising physiologically compatible concentrations of water-soluble or dispersible nutrients and physiological salts; preparing nanoparticles, which are liposomes comprising cholesterol, fatty acids, and cellular growth factors; and emulsifying said base nutritive medium and said nanoparticles to form a two phase composition, wherein said composition has an osmolality of at least about 300 mOsM/kg and

does not contain a cryoprotective agent.

DOCUMENT-IDENTIFIER: US 20070036783 A1

TITLE: ANTIBODY COMPLEXES

----- KWIC -----

Description of Disclosure - DETX (32):

[0041] Non-limiting examples of genetic material encoding a therapeutic agent include polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding antibodies; genes encoding apoptotic or pro-death genes, such as tumor necrosis factor related apoptosis inducing ligand (TRAIL); gene encoding products that inhibit angiogenesis; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoA1 and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; genes allowing for positive selection of cells, such as mutant methyl guanine transferase (MGMT); negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and genes encoding antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes, antisense polynucleotides; polynucleotides encoding micro RNAs and hairpin RNAs for induction of RNAi (RNA interference) such as by use of siRNA (short interfering RNA), aptamers, and/or RNA decoys; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors; genes encoding zinc finger nucleases; and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system.

DOCUMENT-IDENTIFIER: US 20070010016 A1

TITLE: Gene transfer with adenoviruses having modified fiber proteins

----- KWIC -----

Description of Disclosure - DETX (61):

[0070] DNA sequences encoding therapeutic agents include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding G-CSF, GM-CSF, TGF-.alpha., TGF-.beta., and fibroblast growth factor; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; genes encoding co-stimulatory antigens, such as B7.1; genes encoding chemotactic agents, such as lymphotactin, the cystic fibrosis transmembrane conductance regulator (CFTR) genes; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn--SOD), catalase, copper-zinc-superoxide dismutase (CuMn--SOD), extracellular superoxide dismutase (EC--SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; genes encoding anti-angiogenic factors, such as, for example, endothelial monocyte activating polypeptide-2 (EMAP-2); the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; cell cycle control agent genes, such as, for example, the p21 gene; antisense polynucleotides to the cyclin G1 and cyclin D1 genes; the endothelial nitric oxide synthetase (ENOS) gene; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; the dihydrofolate reductase (DHFR) gene; DNA sequences encoding ribozymes;

antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

DOCUMENT-IDENTIFIER: US 20060292166 A1

TITLE: Vaccine composition comprising Flt3-ligand

----- KWIC -----

Description of Disclosure - DETX (22):

[0037] The procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Briefly, the term means a method comprising: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo . In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-ligand, IL-1, IL-3, c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20060292119 A1

TITLE: Modulation of negative immune regulators and
applications for immunotherapy

----- KWIC -----

Description of Disclosure - DETX (287):

[0327] The procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference, can be applied to the cells of the present invention. Other suitable methods are known in the art, therefore the present invention is not limited to any particular method of ex vivo expansion of the cells. Briefly, ex vivo culture and expansion of DCs comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a mammal from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used for culturing and expansion of the cells.

DOCUMENT-IDENTIFIER: US 20060280729 A1

TITLE: Cellular therapy for ocular degeneration

----- KWIC -----

Description of Disclosure - DETX (44):

[0071] Cell lysates or cell soluble fractions prepared from populations of MSC's may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or allogenic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060269519 A1

TITLE: Modulation of cytokine signaling regulators and
applications for immunotherapy

----- KWIC -----

Description of Disclosure - DETX (227):

[0264] The procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference, can be applied to the cells of the present invention. Other suitable methods are known in the art, therefore the present invention is not limited to any particular method of ex vivo expansion of the cells. Briefly, ex vivo culture and expansion of DCs comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a mammal from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used for culturing and expansion of the cells.

DOCUMENT-IDENTIFIER: US 20060264886 A9

TITLE: Method for altering insulin pharmacokinetics

PRIOR-PUBLICATION-INFORMATION:

DOCUMENT-IDENTIFIER DOCUMENT-DATE

US 20050055010 A1 March 10, 2005

----- KWIC -----

Description of Disclosure - DETX (24):

[0061] The present invention provides methods for administering antineoplastic agents. Such antineoplastic agents include a variety of agents including cytokines, angiogenesis inhibitors, classic anticancer agents and therapeutic antibodies. Cytokines immunomodulating agents and hormones that may be used in accordance with the invention include, but are not limited to interferons, interleukins (IL-1, -2, -4, -6, -8, -12) and cellular growth factors.

DOCUMENT-IDENTIFIER: US 20060264409 A1

TITLE: Compositions and methods of treatment for inflammatory diseases

----- KWIC -----

Description of Disclosure - DETX (46):

[0050] Antioxidants, such as NAC, and 5-ASA possess the ability to scavenge oxygen free radicals, inhibit inducible NO formation and to down regulate nuclear factor .kappa..beta. (NF-.kappa..beta.) activity (9, 10, 15-17). Furthermore, antioxidants, such as phenyl N-tert-butyl nitron, and 5-ASA have been shown to inhibit cytokine production, including tumor necrosis factor TNF.alpha., and to retard adhesion molecule expression and B-cell mediated antibody production (10, 18-20) in experimented models of colitis. Separately and together these agents can, thus, be envisioned to moderate immunocyte (T cell) mediated cytokine elaboration, neutrophil generation of ROS and NO, prostaglandin release and to facilitate an environment for unopposed cellular and growth factor-mediated tissue repair. These results show that treatment with the NAC plus 5-ASA combination cause marked improvement in indices of colitis and, furthermore, demonstrate prominent features of epithelial repair, and mucosal architectural and glandular restoration. These data combined with the near normalization of MPO activity and marked reduction in cytokine (IL-A, IL-B, IL-6) expression indicate that therapy with the NAC plus 5-ASA combination exerts a significantly greater anti-inflammatory and reparative effect in TNBS colitis than either 5-ASA or NAC when used alone.

DOCUMENT-IDENTIFIER: US 20060234376 A1

TITLE: Repair and regeneration of ocular tissue using
postpartum-derived cells

----- KWIC -----

Description of Disclosure - DETX (63):

[0090] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060233766 A1

TITLE: Treatment of Parkinson's disease and related disorders
using postpartum derived cells

----- KWIC -----

Description of Disclosure - DETX (76):

[0096] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060233765 A1

TITLE: Treatment of stroke and other acute neuraldegenerative disorders using postpartum derived cells

----- KWIC -----

Description of Disclosure - DETX (72):

[0092] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060212125 A1

TITLE: Bone repairing material using a chondrocyte having the potential for hypertrophy and a scaffold

----- KWIC -----

Description of Disclosure - DETX (78):

[0154] "Growth factor" or "cellular growth factor" as used interchangeably herein, refer to a substance which enhances or controls the induction of the growth and differentiation of cells. Growth factor is also a proliferation or development factor. In cell culture or tissue culture, growth factors can be added to the medium and substituted for the function of macromolecules in serum. It is proved that, in addition to cell growth, many growth factors function as factors that regulate differentiation.

DOCUMENT-IDENTIFIER: US 20060205069 A1

TITLE: Compositions comprising a first agent which provides a primary activation signal to T cells and a second agent which stimulates an accessory molecule on the surface of T cells

----- KWIC -----

Description of Disclosure - DETX (152):

[0147] Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo 10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

DOCUMENT-IDENTIFIER: US 20060194741 A1

TITLE: Dimeric IAP inhibitors

----- KWIC -----

Description of Disclosure - DETX (259):

[0235] Embodiments of the invention also include a method of treating a patient with a condition in need thereof wherein administration of a therapeutically effective amount of a Smac peptidomimetic is delivered to the patient, and the Smac peptidomimetic binds to at least one IAP. In one embodiment the IAP can be XIAP. In another embodiment the IAP can be ML-IAP. In another embodiment the IAP can cIAP-1 or cIAP-2. In a further embodiment the IAP can be multiple IAP types. The method may further include the concurrent administration chemotherapeutic agent. The chemotherapeutic agent can be, but is not limited to, alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I inhibitors, topoisomerase II inhibitors, immunomodulating agents, cellular growth factors, cytokines, and nonsteroidal anti-inflammatory compounds.

Description of Disclosure - DETX (275):

[0251] Additional chemotherapeutic agents. Chemotherapeutic agents suitable for use in combination with the present invention, include but are not limited to the chemotherapeutic agents described in "Modern Pharmacology with Clinical Applications", Sixth Edition, Craig & Stitzel, Chpt. 56, pg 639-656 (2004), herein incorporated by reference in its entirety. This reference describes chemotherapeutic drugs to include alkylating agents, antimetabolites, anti-tumor antibiotics, plant-derived products such as taxanes, enzymes, hormonal agents such as glucocorticoids, miscellaneous agents such as cisplatin, monoclonal antibodies, immunomodulating agents such as interferons, and cellular growth factors. Other suitable classifications for chemotherapeutic agents include mitotic inhibitors and nonsteroidal anti-estrogenic analogs. Other suitable chemotherapeutic agents include topoisomerase I and II inhibitors, kinase inhibitors and any agent capable of activating the extrinsic or intrinsic apoptotic pathway or release of Smac from the mitochondria.

DOCUMENT-IDENTIFIER: US 20060189963 A1

TITLE: MULTI-RESERVOIR DEVICE FOR CONTROLLED DRUG DELIVERY

----- KWIC -----

Description of Disclosure - DETX (38):

[0047] A wide variety of molecules can be contained in and released from the microchip devices. Examples of the molecules include drugs, diagnostic reagents, fragrances, dyes or coloring agents, sweeteners and other flavoring agents, and compounds used in tissue culture, such as cellular growth factors.

DOCUMENT-IDENTIFIER: US 20060189580 A1

TITLE: 1-Adamantyl chalcones for the treatment of
proliferative disorders

----- KWIC -----

Description of Disclosure - DETX (112):

[0124] The compounds of the present invention were evaluated by comparing breast cancer cell lines MCF-7 (ER-positive) and MDA-MB435 (ER-negative) with noncancerous breast epithelial cells (MCF-10). Those compounds that showed a high level of antiproliferative activity against tested breast cancer cell lines, but not against normal breast epithelial cells were evaluated for in vitro mechanism of action by looking at their effects against cellular growth factors, Epidermal Growth Factor (EGF), and Transforming Growth Factor (TGF-alpha).

DOCUMENT-IDENTIFIER: US 20060188983 A1

TITLE: Postpartum-derived cells for use in treatment of
disease of the heart and circulatory system

----- KWIC -----

Description of Disclosure - DETX (108):

[0150] The invention also provides cell lysates, soluble cell fractions and membrane-enriched cell fractions prepared from the populations of the postpartum cells. Such lysates and fractions have many utilities. Use of cell lysates, and more particularly soluble cell fractions, in vivo allows the beneficial intracellular milieu to be used in a patient allogeneic patient without stimulating allogeneic lymphocytes, or generating other adverse immunological responses, or triggering rejection. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their Growth Medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or another solution. For making lysates from cells directly in the growth medium it is preferred that cells are grown in serum from the species in which the lysates are to be used, in some embodiments, washed cells may be preferred. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, enriched, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or, for example, with syngeneic or autologous live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example, needed cellular growth factors to a patient. Preferably, the lysates are not immunogenic, and more preferably they are immunologically tolerated in a broad population of syngeneic and allogeneic recipients without adverse immunological consequences or reaction. Cell lysates of the invention are useful from cells at any stage or age which have been grown under conditions for growth and expansion, for example on Growth Medium. Even senescent cells are useful for the preparation of lysate and can provide certain factors which are biologically useful. Nonviable or even dead or killed cells have utility for preparing lysates, and cellular fractions. Also useful are lysates from cells which have been exposed to factors which tend to induce them along a mesenchymal pathway, particularly towards cardiomyogenic, angiogenic, hemangiogenic, and vasculogenic lines. Cell lysates from differentiated cells, or cells more committed than the PPDCs are also desirable. For example, lysates from cells with characteristics of cardiomyoblasts, cardiomyocytes, angioblasts, hemangioblasts and the like, or

their progenitors are also useful and contemplated for use herewith.

DOCUMENT-IDENTIFIER: US 20060166361 A1

TITLE: Postpartum cells derived from placental tissue, and
methods of making, culturing, and using the same

----- KWIC -----

Description of Disclosure - DETX (183):

[0281] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060159667 A1

TITLE: Rapamycin-resistant T cells and therapeutic uses
thereof

----- KWIC -----

Description of Disclosure - DETX (81):

[0150] A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art. Briefly, ex vivo culture and expansion comprises: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20060154367 A1

TITLE: Cartilage and bone repair and regeneration using
postpartum-derived cells

----- KWIC -----

Description of Disclosure - DETX (250):

[0275] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060154366 A1

TITLE: Treatment of osteochondral diseases using
postpartum-derived cells and products thereof

----- KWIC -----

Description of Disclosure - DETX (180):

[0277] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of freeze-thaw disruption, osmotic disruption, mechanical disruption, ultrasonic disruption, enzymatic disruption (e.g., hyaluronidase, dispase, proteases, and nucleases (for example, deoxyribonuclease and ribonuclease)), or chemical disruption (non-ionic detergents such as, for example, alkylaryl polyether alcohol (TRITON.RTM. X-100), octylphenoxy polyethoxy-ethanol (Rohm and Haas Philadelphia, Pa.), BRIJ-35, a polyethoxyethanol lauryl ether (Atlas Chemical Co., San Diego, Calif.), polysorbate 20 (TWEEN 20.RTM.), a polyethoxyethanol sorbitan monolaureate (Rohm and Haas), polyethylene lauryl ether (Rohm and Haas); and ionic detergents such as, for example, sodium dodecyl sulphate, sulfated higher aliphatic alcohols, sulfonated alkanes and sulfonated alkylarenes containing 7 to 22 carbon atoms in a branched or unbranched chain), or combinations thereof. Cells may also be lysed on their growth substrate. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. In some embodiments, cellular membranes are removed from the lysate, for example by centrifugation, ultracentrifugation, filtration, chromatograph, or sedimentation, to yield a membrane fraction and supernate fraction. The membrane fraction or the supernate may be used according to the methods of the invention. In some embodiments, cellular debris is removed by treatment with a mild detergent rinse, such as EDTA, CHAPS or a zwitterionic detergent. Cell lysates may be used in vitro or in vivo, alone or, for example, with cells or on a substrate. The cell lysates, if introduced in vivo, may be introduced locally at a site of

treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060154365 A1

TITLE: Cultured three dimensional tissues and uses thereof

----- KWIC -----

Description of Disclosure - DETX (92):

[0100] The three dimensional tissues herein produce various cellular growth factors that affect, among others, cell proliferation, differentiation, and recruitment. The three dimensional tissues described herein may be used to deliver the suite or repertoire of growth factors to desired cells, tissues, or organs, or used to produce growth factors for isolation. In some embodiments, the growth factor is delivered by the compositions comprise VEGF, which induces vascular permeability, promotes growth and survival of vascular endothelial cells, and controls hematopoietic stem cell survival. In vivo, VEGF promotes angiogenesis and the formation of new blood vessels.

DOCUMENT-IDENTIFIER: US 20060153818 A1

TITLE: Cartilage and bone repair and regeneration using
postpartum-derived cells

----- KWIC -----

Description of Disclosure - DETX (250):

[0275] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060153817 A1

TITLE: Cartilage and bone repair and regeneration using
postpartum-derived cells

----- KWIC -----

Description of Disclosure - DETX (250):

[0281] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060153816 A1

TITLE: Soft tissue repair and regeneration using
postpartum-derived cells and cell products

----- KWIC -----

Description of Disclosure - DETX (178):

[0282] Cell fractions prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions or supernatants in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of freeze-thaw disruption, osmotic disruption, mechanical disruption, ultrasonic disruption, enzymatic disruption (e.g., hyaluronidase, dispase, proteases, and nucleases (for example, deoxyribonuclease and ribonuclease)), or chemical disruption (non-ionic detergents such as, for example, alkylaryl polyether alcohol (TRITON.RTM. X-100), octylphenoxy polyethoxy-ethanol (Rohm and Haas Philadelphia, Pa.), BRIJ-35, a polyethoxyethanol lauryl ether (Atlas Chemical Co., San Diego, Calif.), polysorbate 20 (TWEEN 20.RTM.), a polyethoxyethanol sorbitan monolaureate (Rohm and Haas), polyethylene lauryl ether (Rohm and Haas); and ionic detergents such as, for example, sodium dodecyl sulphate, sulfated higher aliphatic alcohols, sulfonated alkanes and sulfonated alkylarenes containing 7 to 22 carbon atoms in a branched or unbranched chain), or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Cells may also be lysed on their growth substrate. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. In some embodiments, cellular membranes are removed from the lysate, for example by centrifugation, or ultracentrifugation, filtration, chromatograph, or sedimentation, to yield a membrane fraction and supernate fraction. The membrane fraction or the supernate may be used according to the methods of the invention. In some embodiments, cellular debris is removed by treatment with a mild detergent rinse, such as EDTA, CHAPS or a zwitterionic detergent. Cell lysates may be used in vitro or in vivo, alone or, for example, with cells or on a substrate. The cell lysates, if introduced in vivo, may be introduced

locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20060148737 A1

TITLE: Wound healing method and kits

----- KWIC -----

Abstract Paragraph - ABTX (1):

Electroporation is used to enhance the wound-healing benefit provided by transfection of nucleic acids that encode cellular growth factors. Wounds which are amenable to the method include inter alia cutaneous lesions, muscular lesions, osseous lesions, burn wounds, and gastrointestinal anastomoses. Kits comprise electrodes and nucleic acids encoding cellular growth factors.

DOCUMENT-IDENTIFIER: US 20060141057 A1

TITLE: Methods of treatment of inflammatory diseases

----- KWIC -----

Description of Disclosure - DETX (46):

[0049] Antioxidants, such as NAC, and 5-ASA possess the ability to scavenge oxygen free radicals, inhibit inducible NO formation and to down regulate nuclear factor .kappa.B (NF-.kappa.B) activity (9, 10, 15-17). Furthermore, antioxidants, such as phenyl N-tert-butyl nitron, and 5-ASA have been shown to inhibit cytokine production, including tumor necrosis factor TNF.alpha., and to retard adhesion molecule expression and B-cell mediated antibody production (10, 18-20) in experimented models of colitis. Separately and together these agents can, thus, be envisioned to moderate immunocyte (T cell) mediated cytokine elaboration, neutrophil generation of ROS and NO, prostaglandin release and to facilitate an environment for unopposed cellular and growth factor-mediated tissue repair. These results show that treatment with the NAC plus 5-ASA combination cause marked improvement in indices of colitis and, furthermore, demonstrate prominent features of epithelial repair, and mucosal architectural and glandular restoration. These data combined with the near normalization of MPO activity and marked reduction in cytokine (ILa, ILb, IL6) expression indicate that therapy with the NAC plus 5-ASA combination exerts a significantly greater anti-inflammatory and reparative effect in TNBS colitis than either 5-ASA or NAC when used alone.

DOCUMENT-IDENTIFIER: US 20060140919 A1

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Description of Disclosure - DETX (91):

[0096] Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

DOCUMENT-IDENTIFIER: US 20060134157 A1

TITLE: Co-continuous phase composite polymer blends for
in-vivo and in-vitro biomedical applications

----- KWIC -----

Brief Summary Text - BSTX (19):

[0018] The co-continuous polymer blend technology allows for the incorporation of substances into one or more of the polymers at the blend interface to promote bone or tissue growth, such as cell attachment mediators, osteoinductive substances, cellular growth factors, other nutrients and pharmaceuticals, and the like. Particulate materials that promote bone or tissue growth may also be used, such as hydroxyapatite or tricalcium phosphate. Therefore, tissue-compatible polymer composites according to the present invention will also include composites containing one or more substances or particles that promote bone or tissue ingrowth, nutrient substances, pharmaceutical substances, and the like.

DOCUMENT-IDENTIFIER: US 20060134118 A1

TITLE: Methods for regulating cancer

----- KWIC -----

Brief Summary Text - BSTX (5):

[0003] Several genes have been implicated in various cancers. For instance, oncogenes are known to code for receptors for cellular growth factor such as epidermal growth factor. The ras gene is an oncogene that is believed to be responsible for up to 90% of all human pancreatic cancer, 50% of human colon cancers, 40% of lung cancers, and 30% of leukemias. Mutated oncogenes can become cancer-causing genes. Such mutated oncogenes code for proteins such as protein kinases and protein phosphorylating enzymes that trigger uncontrolled cell growth. EphB4 is a recently identified member of the largest known family of receptor protein tyrosine kinases. Eph receptor family members have been identified to be involved in many cellular processes including neural development, angiogenesis and vascular network assembly (2-5). As a result of interactions with their ligands, the ephrins, they mediate contact-dependent cell interactions, which regulate cell functions such as contact inhibition, cytoskeletal organisation and cell migration (6, 7).

DOCUMENT-IDENTIFIER: US 20060127503 A1

TITLE: Compositions for treatment of inflammatory diseases

----- KWIC -----

Description of Disclosure - DETX (46):

[0050] Antioxidants, such as NAC, and 5-ASA possess the ability to scavenge oxygen free radicals, inhibit inducible NO formation and to down regulate nuclear factor .kappa.B (NF-.kappa.B) activity (9, 10, 15-17). Furthermore, antioxidants, such as phenyl N-tert-butyl nitron, and 5-ASA have been shown to inhibit cytokine production, including tumor necrosis factor TNF.alpha., and to retard adhesion molecule expression and B-cell mediated antibody production (10, 18-20) in experimented models of colitis. Separately and together these agents can, thus, be envisioned to moderate immunocyte (T cell) mediated cytokine elaboration, neutrophil generation of ROS and NO, prostaglandin release and to facilitate an environment for unopposed cellular and growth factor-mediated tissue repair. These results show that treatment with the NAC plus 5-ASA combination cause marked improvement in indices of colitis and, furthermore, demonstrate prominent features of epithelial repair, and mucosal architectural and glandular restoration. These data combined with the near normalization of MPO activity and marked reduction in cytokine (ILa, ILb, IL6) expression indicate that therapy with the NAC plus 5-ASA combination exerts a significantly greater anti-inflammatory and reparative effect in TNBS colitis than either 5-ASA or NAC when used alone.

DOCUMENT-IDENTIFIER: US 20060122114 A1

TITLE: Antibodies to heregulin 2

----- KWIC -----

Brief Summary Text - BSTX (9):

[0009] Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B 1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

DOCUMENT-IDENTIFIER: US 20060116904 A1

TITLE: Wound electronic medical record system

----- KWIC -----

Description of Disclosure - DETX (73):

[0082] Wound debridements and applications of Apligraf or other biologics are also tracked, and new dates entered, by pressing the "Debridements and Apligraf" button 624. This brings up form 800, shown in FIG. 8. A new debridement date can be entered in the blank record 802, along with check boxes for the appropriate data such as Debridement, Apligraf, OR (if procedure was performed in the operating room) and Bedside (if the procedure was performed at the bedside (or in clinic). Other selections, based on different protocols or treatment options, can be readily added to this form and created in the table space. For example, other FDA approved biologicals for use in healing diabetic foot ulcers currently include Regranex and Dermagraft. Since different cellular and growth factor therapies are distinct and function by sharply different mechanisms, the protocol design rules for data entry can be used to prompt different options, based on the other wound characteristics already selected. For example, common to the three biologicals noted here is the requirement that they should not be used in the presence of drainage, infection, or without debridement. If the selections entered for these values is contrary, an alert can be provided to the user, prompting correction of other data entered, or reconsideration of a proposed therapy.

DOCUMENT-IDENTIFIER: US 20060103807 A1

TITLE: Ophthalmic and ophthalmological use of a complex nutritive base in an aqueous medium

----- KWIC -----

Brief Summary Text - BSTX (7):

[0011] To be effective, culture media of the above kind incorporate cellular growth factors, which may already be present in the composition of the culture medium at the outset or may be produced during culturing, e.g. by a feeder strain of fibroblasts, it being a question of the culturing of keratinocytes.

Description of Disclosure - DETX (3):

[0029] In the present invention, the trophic composition in an aqueous medium which may be utilized comprises: [0030] a complex nutritive base comprising at least a multiplicity of amino acids, vitamins, trace elements, and metallic salts, the said base being free of any cellular growth factor, any biological extract of animal or cellular origin, or any therapeutic active principle, [0031] an inhibitor of collagenases of the human or animal corneal epithelium, and [0032] a promoter of neocollagen synthesis.

Claims Text - CLTX (1):

1. The use of a complex nutritive base in an aqueous medium, the said base comprising at least a multiplicity of amino acids, vitamins, trace elements, and metallic salts and being free of any cellular growth factor or any biological extract of animal or cellular origin or any pharmaceutically active principle, as an ophthalmologic medicine or ophthalmic solution for application in external contact with the eye in man or in animals.

Claims Text - CLTX (2):

2. The use of a complex nutritive base in an aqueous, medium, the said base comprising at least a multiplicity of amino acids, vitamins, trace elements, and metallic salts and being free of any cellular growth factor or any biological extract of animal or cellular origin or any pharmaceutically active principle, as a treatment product for the storage, preservation, transport, or placement of items or prostheses, such as contact lenses, which are designed to come into external contact with the cornea of the eye in man or in animals.

DOCUMENT-IDENTIFIER: US 20060099177 A1

TITLE: Methods for treating HIV infected subjects

----- KWIC -----

Description of Disclosure - DETX (171):

[0169] Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

DOCUMENT-IDENTIFIER: US 20060094082 A1

TITLE: Composition of lactoferrin related peptides and uses thereof

----- KWIC -----

Description of Disclosure - DETX (210):

[0236] A wound is also further defined as a chronic wound. Examples of chronic wounds or chronic ulcers include, but are not limited to diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Yet further, chronic wounds can also include infected wounds. Chronic wounds are wounds that do not repair or do so extremely slowly, and show partial or total lack of structural organization and functional coordination with normal tissue. Chronic wounds or chronic ulcers can be broadly classified into three major types: diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Diabetic ulcers often occur on a foot. Chronic diabetic state and poor glucose control results in poor peripheral circulation and microcirculation due to progressive arteriosclerosis; neuropathic changes that result in an insensate extremity prone to trauma; and intrinsic defects in the wound healing process that may include reduced abundance and response to cellular growth factors. In the case of venous ulcers, venous hypertension causes disturbed microcirculation and pathological changes of the capillaries, elevated persistent levels of pro-inflammatory cytokines and proteases. Fibroblast senesce and respond less to growth factors, which distribute unfavorably. Proteolytic enzymes and their inhibitors are imbalanced. Pressure ulcers occur when skin is under pressure without movement to allow blood flow for 8-12 hours.

DOCUMENT-IDENTIFIER: US 20060089673 A1

TITLE: Germicidal method for treating or preventing sinusitis

----- KWIC -----

Brief Summary Text - BSTX (45):

[0044] In most if not all cases the treatment includes the step of destroying biofilm in or on the treated tissue or region, wherein the treated tissue or region activates or otherwise stimulates stem cells or release of cellular growth factors in the sinus or nasal structure effecting a tissue repair or tissue regeneration.

Claims Text - CLTX (12):

12. The method of claim 8 wherein the treated tissue or region activates or otherwise stimulates stem cells or release of cellular growth factors in the nasal or sinus structure effecting a tissue repair or tissue regeneration.

DOCUMENT-IDENTIFIER: US 20060078989 A1

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Brief Summary Text - BSTX (11):

[0010] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) isolating the monocytes from human blood; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (12):

[0011] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) providing human monocytes; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (17):

[0016] The present invention includes and provides a dedifferentiated, programmable stem cell of human monocytic origin manufactured by a process comprising (a) isolating monocytes from human blood; (b) propagating monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Claims Text - CLTX (2):

35. A process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising: a) isolating monocytes from human blood; b) propagating said monocytes in a culture medium comprising cellular growth factor M-CSF; and c) cultivating said monocytes simultaneously with or subsequently to step b) in a culture medium comprising IL-3.

Claims Text - CLTX (16):

49. A process for the production of dedifferentiated, programmable stem cells of human monocytic origin in a pharmaceutical preparation, comprising: a) isolating monocytes from human blood; b) propagating said monocytes in a culture medium comprising cellular growth factor M-CSF; c) cultivating said monocytes simultaneously with or subsequently to step b) in a culture medium

comprising IL-3; d) obtaining dedifferentiated, programmable stem cell of human monocytic origin from said culture medium comprising IL-3; and e) formulating a pharmaceutical preparation in a suitable medium, wherein said pharmaceutical preparation is derived from said human adult dedifferentiated programmable stem cell.

Claims Text - CLTX (17):

50. A process for preparing a dedifferentiated, programmable stem cell of human monocytic origin for introduction into a body, comprising: a) isolating monocytes from human blood; b) propagating said monocytes in a culture medium comprising cellular growth factor M-CSF; c) cultivating said monocytes simultaneously with or subsequently to step b) in a culture medium comprising IL-3; d) obtaining dedifferentiated, programmable stem cells of human monocytic origin from said culture medium comprising IL-3; and e) applying said dedifferentiated, programmable stem cell of human monocytic origin to a material.

DOCUMENT-IDENTIFIER: US 20060078980 A1

TITLE: Production of polyketides and other natural products

----- KWIC -----

Description of Disclosure - DETX (332):

[0559] Alarcon, C. M., Heitman, J., and Cardenas, M. E. (1999) Protein kinase activity and identification of a toxic effector domain of the target of rapamycin TOR proteins in yeast. *Molecular Biology of the Cell* 10: 2531-2546. [0560] Aparicio, J. F., Molnar, I., Schwecke, T., Konig, A., Haydock, S. F., Khaw, L. E., Staunton, J., and Leadlay, P. F. (1996) Organization of the biosynthetic gene cluster for rapamycin in *Streptomyces hygroscopicus*: analysis of the enzymatic domains in the modular polyketide synthase. *Gene* 169: 9-16. [0561] Baker, H., Sidorowicz, A., Sehgal, S. N., and Vezina, C. (1978) Rapamycin (AY-22,989), a new antifungal antibiotic. III. In vitro and in vivo evaluation. *Journal of Antibiotics* 31: 539-545. [0562] Bierman, M., Logan, R., O'Brien, K., Seno, E. T., Nagaraja Rao, R., and Schoner, B. E. (1992) Plasmid cloning vectors for the conjugal transfer of DNA from *Escherichia coli* to *Streptomyces* spp. *Gene* 116: 43-49. [0563] Blanc, V., Lagneaux, D., Didier, P., Gil, P., Lacroix, P., and Crouzet, J. (1995) Cloning and analysis of structural genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the conversion of pristinamycin II.sub.B to pristinamycin II.sub.A (PII.sub.A): PII.sub.A synthase and NADH:riboflavin 5'-phosphate oxidoreductase. *Journal of Bacteriology* 177: 5206-5214. [0564] Blanc, V., Gil, P., Bamas-Jacques, N., Lorenzon, S.; Zagorec, M., Schleuniger, J., Bisch, D., Blanche, F., Debussche, L., Crouzet, J., and Thibaut, D. (1997) Identification and analysis of genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the biosynthesis of the 4-dimethylamino-L-phenylalanine precursor of pristinamycin I. *Molecular Microbiology* 23: 191-202. [0565] Box, S. J., Shelley, P. R., Tyler, J. W., Verrall, M. S., Warr, S. R. C., Badger, A. M., Levy, M. A., and Banks, R. M. (1995) 27-O-Demethylrapamycin, an immunosuppressant compound produced by a new strain of *Streptomyces hygroscopicus*. *Journal of Antibiotics* 48:1347-1349. [0566] Brown, E. J., Albers, M. W., Shin, T. B., Ichikawa, K., Keith, C. T., Lane, W. S., and Schreiber, S. L. (1994) A mammalian protein targeted by G1-arresting rapamycin-receptor complex. *Nature* 369: 756-758. [0567] Brunn, G. J., Williams, J., Sabers, C., Wiederrecht, G., Lawrence, J. C., and Abraham, R. T. (1996) Direct inhibition of the signaling functions of the mammalian target of rapamycin by the phosphoinositide 3-kinase inhibitors, wortmannin and LY294002. *EMBO Journal* 15: 5256-5267. [0568] Cao, W., Mohacsi, P., Shorthouse, R., Pratt, R. and Morris, R. E. (1995). Effects of rapamycin on growth factor-stimulated vascular smooth muscle cell DNA synthesis. Inhibition of basic fibroblast growth factor and platelet-derived growth factor action and antagonism of rapamycin by FK506. *Transplantation* 59(3): 390-395. [0569] Carlson, R. P., Hartman, D. A., Tomchek, L. A., Walter, T. L., Lugay, J. R., Calhoun, W., Sehgal, S. N., Chang, J. Y. (1993). Rapamycin, a potential

disease-modifying antiarthritic drug. *J. Pharmacol. Exp. Ther.* 266(2):1125-38. [0570] Chambraud, B., Radanyi, C., Camonis, J. H., Shazand, K., Rajkowski, K., and Baulieu, E. E. (1996) FAP48, a new protein that forms specific complexes both immunophilins FKBP59 and FKBP12. Prevention by the immunosuppressant drugs FK506 and rapamycin. *Journal of Biological Chemistry* 271: 32923-32929. [0571] Chang, J. Y., Sehgal, S. N., and Bansbach, C. C. (1991) FK506 and rapamycin: novel pharmacological probes of the immune response. *Trends in Pharmacological Sciences* 12: 218-223. [0572] Chen, J., Zheng, X. F., Brown, E. J., and Schreiber, S. L. (1995) Identification of an 11-kDa FKBP12-rapamycin-binding domain within the 289-kDa FKBP12-rapamycin-associated protein and characterization of a critical serine residue. *Proceedings of the National Academy of Sciences of the United States of America* 92: 4947-4951. [0573] Chini, M., Crotti, P., Gardelli, C., and Macchia, F., (1992), *Tetrahedron*, 48, 3805-3812 [0574] Choi, J. W., Chen, J., Schreiber, S. L., and Clardy, J. (1996) Structure of the FKBP12-rapamycin complex interacting with the binding domain of human FRAP. *Science* 273: 239-242. [0575] Chung, L., Liu, L., Patel, S., Carney, J. R., and Reeves, C. D. (2001) Deletion of rapQNM from the rapamycin gene cluster of *Streptomyces hygroscopicus* gives production of the 16-O-desmethyl-27-desmethoxy analog. *Journal of Antibiotics* 54: 250-256. [0576] Corey, E. J. and Huang, H., (1989) *Tetrahedron Lett.*, 30, 5235-5238 [0577] DiLella, A. G., and Craig, R. J. (1991) Exon organization of the human FKBP-12 gene: correlation with structural and functional protein domains. *Biochemistry* 30: 8512-8517. [0578] Du, L. C., Sanchez, C., Chen, M., Edwards, D. J., and Shen, B. (2000) The biosynthetic gene cluster for the antitumor drug bleomycin from *Streptomyces verticillus* ATCC15003 supporting functional interactions between nonribosomal peptide synthetases and a polyketide synthase. *Chemistry & Biology* 7: 623-642. [0579] Dudkin, L., Dilling, M. B., Cheshire, P. J., Harwood, F. C., Hollingshead, M., Arbuck, S. G., Travis, R., Sausville, E. A., Houghton, P. J. (2001). Biochemical correlates of mTOR inhibition by the rapamycin ester CCI-779 and tumor growth inhibition. *Clin. Cancer Res.* 7(6):1758-64 [0580] Fehr, T., Sanglier, J-J., Schuler, W., Gschwind, L., Ponelle, M., Schilling, W., Wioland, C. (1996). Antascomicin A, B, C, D and E: Novel FKBP12 binding compounds from a *Micromonospora* strain. *J. Antibiot.* 49(3): 230-233. [0581] Ferrari, S., Pearson, R. B., Siegmann, M., Kozma, S. C., and Thomas, G. (1993) The immunosuppressant rapamycin induces inactivation of P70.sup.s6k through dephosphorylation of a novel set of sites. *Journal of Biological Chemistry* 268: 16091-16094. [0582] Findlay J. A, and Radics, L. (1980) *Canadian Journal of Chemistry* 58:579. [0583] Fishbein, T. M., Florman, S., Gondolesi, G., Schiano, T., LeLeiko, N., Tschernia, A., Kaufman, S. (2002). Intestinal transplantation before and after the introduction of sirolimus. *Transplantation*. 73(10): 1538-42. [0584] Foey, A., Green, P., Foxwell, B., Feldmann, M., Brennan, F. (2002). Cytokine-stimulated T cells induce macrophage IL-10 production dependent on phosphatidylinositol 3-kinase and p70S6K: implications for rheumatoid arthritis. *Arthritis Res.* 4(1):64-70. Epub 2001 Oct. 10. [0585] Gaisser, S., Reather, J., Wirtz, G., Kellenberger, L., Staunton, J., and Leadlay, P. F. (2000) A defined system for hybrid macrolide biosynthesis in *Saccharopolyspora erythraea*. *Molecular Microbiology* 36: 391-401. [0586] Gaisser, S., Lill, R., Staunton, J., Mendez, C., Salas,

J., Leadlay, P F. (2002) Parallel pathways for oxidation of 14-membered polyketide macrolactones in *Saccharopolyspora erythraea*. *Mol Microbiol* 44:771-81. [0587] Galat, A. (2000) Sequence diversification of the FK506-binding proteins in several different genomes. *European Journal of Biochemistry* 267: 4945-4959. [0588] Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular growth factor and cytokine response in injured vessels. *Transplantation* 55(6):1409-1418. [0589] Gregory M A, Till R, Smith, M C M. (in Press) Integration site for *Streptomyces* phage .phi.BT1 and the development of site-specific integrating vectors. *J. Bacteriol.* [0590] Guba, M., von Breitenbuch, P., Steinbauer, M., Koehl, G., Flegel, S., Hornung, M., Bruns, C. J., Zuelke, C., Farkas, S., Anthuber, M., Jauch, K. W., and Geissler, E. K; (2002) Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. *Nature Medicine* 8: 128-135. [0591] Hamilton, G. S., and Steiner, J. P. (1998) Immunophilins: Beyond immunosuppression. *Journal of Medicinal Chemistry* 41: 5119-5143. [0592] Hara, K., Yonezawa, K., Kozlowski, M. T., Sugimoto, T., Andrabi, K., Weng, Q. P., Kasuga, M., Nishimoto, I., and Avruch, J. (1997) Regulation of eIF4E BP1 phosphorylation by mTOR. *Journal of Biological Chemistry* 272: 26457-26463. [0593] Hardwick, J. S., Kuruvilla, F. G., Tong, J. K., Shamji, A. F., and Schreiber, S. L. (1999) Rapamycin-modulated transcription defines the subset of nutrient-sensitive signaling pathways directly controlled by the Tor proteins. *Proceedings of the National Academy of Sciences of the United States of America* 96: 14866-14870. [0594] Hatanaka, H., Kino, T., Miyata, S., Inamura, N., Kuroda, A., Goto, T., Tanaka, H., Okuhara, M. (1988). FR-900520 and FR-900523, novel immunosuppressants isolated from a *Streptomyces*. II. Fermentation; isolation and physico-chemical and biological characteristics. *J. Antibiot. (Tokyo)*. 41(11):1592-601. [0595] Hatanaka H, Kino T, Asano M, Goto T, Tanaka H, Okuhara M. (1989). FK-506 related compounds produced by *Streptomyces tsukubaensis* No. 9993. *J. Antibiot. (Tokyo)*. 42(4):620-2. [0596] Hendrickson, B. A., Zhang, W., Craig, R. J., Jin, Y. J., Bierer, B. E., Burakoff, S., and DiLella, A. G. (1993) Structural organization of the genes encoding human and murine FK506-binding protein (FKBP) 13 and comparison to FKBP1. *Gene* 134: 271-275. [0597] Hentges, K. E., Sirry, B., Gingeras, A. C., Sarbassov, D., Sonenberg, N., Sabatini, D., and Peterson, A. S. (2001) FRAP/mTOR is required for proliferation and patterning during embryonic development in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 98: 13796-13801. [0598] Hopwood, D. A. (1997) Genetic contributions to understanding polyketide synthases. *Chemical Reviews* 97: 2465-2497. [0599] Hosted, T. J., and Baltz, R. H. (1997) Use of rpsL for dominance selection and gene replacement in *Streptomyces roseosporus*. *Journal of Bacteriology* 179: 180-186. [0600] Hung, D. T., and Schreiber, S. L. (1992) cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein. *Biochemical and Biophysical Research Communications* 184: 733-738. [0601] Hung, D. T., Jamison, T. F., and Schreiber, S. L. (1996) Understanding and controlling the cell cycle with natural products. *Chemistry & Biology* 3: 623-639. [0602] Jain, S., Bicknell, G. R., Whiting, P. H., Nicholson, M. L. (2001). Rapamycin reduces expression of fibrosis-associated

genes in an experimental model of renal ischaemia reperfusion injury. *Transplant Proc.* 33(1-2):556-8. [0603] Jin, Y. J., Burakoff, S. J., and Bierer, B. E. (1992) Molecular cloning of a 25 kDa high affinity rapamycin binding protein, FKBP25. *Journal of Biological Chemistry* 267: 10942-10945. [0604] Kahan, B. D., Chang, J. Y., and Sehgal, S. N. (1991) Preclinical evaluation of a new potent immunosuppressive agent, rapamycin. *Transplantation* 52: 185-191. [0605] Kahan, B. D., and Camardo, J. S. (2001) Rapamycin: Clinical results and future opportunities. *Transplantation* 72:1181-1193. [0606] Kallen, J. A., Sedrani, R., and Cottens S. (1996) X-ray crystal structure of 28-O-methylrapamycin complexed with FKBP12: Is the cyclohexyl moiety part of the effector domain of rapamycin? *Journal of the American Chemical Society* 118: 5857-5861. [0607] Kawasome, H., Papst, P., Webb, S., Keller, G. M., Johnson, G. L., Gelfand, E. W., and Terada, N. (1998) Targeted disruption of p70.s6k defines its role in protein synthesis and rapamycin sensitivity. *Proceedings of the National Academy of Sciences of the United States of America* 95: 5033-5038. [0608] Khaw, L. E., Bohm, G. A., Metcalfe, S., Staunton, J., and Leadlay, P. F. (1998) Mutational biosynthesis of novel rapamycins by a strain of *Streptomyces hygroscopicus* NRRL 5491 disrupted in rapL, encoding a putative lysine cyclodeaminase. *Journal of Bacteriology* 180: 809-814. [0609] Kieser, T., Bibb, M. J., Buttner, M. J., Chater, K. F., and Hopwood, D. A. (2000) *Practical Streptomyces Genetics*, John Innes Foundation, Norwich. [0610] Kirby, B., and Griffiths, C. E. M. (2001) Psoriasis: the future. *British Journal of Dermatology* 144:37-43. [0611] Kirchner, G. I., Winkler, M., Mueller L., Vidal, C., Jacobsen, W., Franzke, A., Wagner, S., Blick, S., Manns M. P., and Sewing K.-F. (2000) Pharmacokinetics of SDZ RAD and cyclosporin including their metabolites in seven kidney graft patients after the first dose of SDZ RAD. *British Journal of Clinical Pharmacology* 50:449-454. [0612] Konig, A., Schwecke, T., Molnar, I., Bohm, G., Lowden, P. A. S., Staunton, J., and Leadlay, P. F. (1997) The pipecolate-incorporating enzyme for the biosynthesis of the immunosuppressant rapamycin. Nucleotide sequence analysis, disruption and heterologous expression of rapP from *Streptomyces hygroscopicus*. *European Journal of Biochemistry* 247: 526-534. [0613] Kunz, J., Loeschmann, A., Deuter-Reinhard, M., and Hall, M. N. (2000) FAP1, a homologue of human transcription factor NF-X1, competes with rapamycin for binding to FKBP12 in yeast. *Molecular Microbiology* 37: 1480-1493. [0614] Kuo, C. J., Chung, J. K., Fiorentino, D. F., Flanagan, W. M., Blenis, J., and Crabtree, G. R. (1992) Rapamycin selectively inhibits interleukin-2 activation of p70 S6 kinase. *Nature* 358: 70-73. [0615] Lee, M. H. Pascopella, L., Jacobs, W. R., Jr and Hatfull, G. F (1991). Site specific integration of mycobacteriophage L5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis* and *Bacille Calmette-Guerin*. *Proc. Natl. Acad. Sci. USA*, 88:3111-3115. [0616] Lee M H, Pascopella L, Jacobs W R Jr, Hatfull G F. (1991), Site-specific integration of mycobacteriophage L5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis*, and *bacille Calmette-Guerin*. *Proc Natl Acad Sci USA.*; 88:3111-5. [0617] Liang, J., Choi, J., and Clardy, J. (1999) Refined structure of the FKBP12-rapamycin-FRB ternary complex at 2.2 Å resolution. *Acta Crystallographica Section D-Biological Crystallography* 55: 736-744. [0618] Lomovskaya, N., Fonstein, L., Ruan, X., Stassi, D., Katz, L., and Hutchinson,

C. R. (1997) Gene disruption and replacement in the rapamycin-producing *Streptomyces hygroscopicus* strain ATCC 29253. *Microbiology-Uk* 143: 875-883.

[0619] Lowden, P. A. S., Bohm, G., Staunton, J., and Leadlay, P. F. (1996) The nature of the starter unit for the rapamycin polyketide synthase. *Angewandte Chemie* 35: 2249-2251. [0620] Lowden, P. A. S., (1997) Ph.D. Dissertation, University of Cambridge. "Studies on the biosynthesis of rapamycin". [0621] Lowden, P. A. S., Wilkinson, B., Bohm, G. A., Handa, S., Floss, H. G., Leadlay, P. F., and Staunton, J. (2001) Origin and true nature of the starter unit for the rapamycin polyketide synthase. *Angewandte Chemie-International Edition* 40: 777-779. [0622] Luengo, J. I., Yamashita, D. S., Dunnington, D., Beck, A. K., Rozamus, L. W., Yen, H. K., Bossard, M. J., Levy, M. A., Hand, A., Newmantarr, T., Badger, A., Faucette, L., Johnson, R. K., Dalessio, K., Porter, T., Shu, A. Y. L., Heys, R., Choi, J. W., Kongsaree, P., Clardy, J., and Holt, D. A. (1995) Structure-Activity Studies of Rapamycin Analogs

DOCUMENT-IDENTIFIER: US 20060073159 A1

TITLE: Human anti-cancer immunotherapy

----- KWIC -----

Description of Disclosure - DETX (167):

[0206] The procedure for ex vivo expansion of hematopoietic stem and progenitor cells described in U.S. Pat. No. 5,199,942, incorporated herein by reference, can be applied to the cells of the present invention. Other suitable methods are known in the art, therefore the present invention is not limited to any particular method of ex vivo expansion of the cells. Briefly, ex vivo culture and expansion of DCs comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a mammal from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used for culturing and expansion of the cells.

DOCUMENT-IDENTIFIER: US 20060057553 A1

TITLE: Chimeric viral vectors for gene therapy

----- KWIC -----

Description of Disclosure - DETX (46):

[0083] DNA sequences encoding therapeutic agents which may be contained in the vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF .alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tpA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell cell antigen receptor; the multidrug resistance (MDR) gene; DNA sequences encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotension converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

DOCUMENT-IDENTIFIER: US 20060057120 A1

TITLE: Administration of dendritic cells partially matured in vitro for the treatment of tumors

----- KWIC -----

Description of Disclosure - DETX (13):

[0025] Monocytic dendritic cell precursors and cell populations enriched for the precursors can be cultured ex vivo for differentiation, and partial maturation and/or expansion. As used herein, isolated immature dendritic cells, dendritic cell precursors, and other cells, refers to cells that, by human hand, exist apart from their native environment, and are therefore not a product of nature. Isolated cells can exist in purified form, in semi-purified form, or in a non-native environment. Briefly, ex vivo differentiation typically involves culturing monocytic dendritic cell precursors, or populations of cells having dendritic cell precursors, in the presence of one or more differentiation agents. Suitable differentiating agents can include, for example, cellular growth factors (e.g., cytokines such as (GM-CSF), Interleukin 4 (IL4), Interleukin 7 (IL-7), Interleukin 13 (IL-13), and/or combinations thereof). In certain embodiments, the monocytic dendritic cells precursors are differentiated to form monocyte-derived immature dendritic cells.

DOCUMENT-IDENTIFIER: US 20060036194 A1

TITLE: Method of treatment for and prevention of periodontal disease

----- KWIC -----

Brief Summary Text - BSTX (18):

[0016] In most if not all cases the treatment includes the step of destroying biofilm in or on the treated tissue or region, wherein the treated tissue or region activates or otherwise stimulates stem cells or release of cellular growth factors in the oral structure effecting a tissue repair or tissue regeneration.

Claims Text - CLTX (12):

12. The method of claim 9 wherein the treated tissue or region activates or otherwise stimulates stem cells or release of cellular growth factors in the oral structure effecting a tissue repair or tissue regeneration.

DOCUMENT-IDENTIFIER: US 20060019394 A1

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Description of Disclosure - DETX (69):

[0085] Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

DOCUMENT-IDENTIFIER: US 20060013832 A1

TITLE: Methods for treating HIV infected subjects

----- KWIC -----

Description of Disclosure - DETX (166):

[0169] Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

DOCUMENT-IDENTIFIER: US 20060003452 A1

TITLE: Vector packaging cell line

----- KWIC -----

Description of Disclosure - DETX (22):

[0050] Non-limiting examples of genetic material encoding a therapeutic agent include polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and genes encoding antioxidants such as, but not limited to, manganese superoxide dismutase (Mn--SOD), catalase, copper-zinc-superoxide dismutase (CuZn--SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system.

DOCUMENT-IDENTIFIER: US 20050287155 A1

TITLE: Conjugates with reduced adverse systemic effects

----- KWIC -----

Detail Description Paragraph - DETX (6):

[0043] In another preferred embodiment, the targeting moiety T is a cellular growth factor. Preferred examples of such growth factors include but are not limited to epidermal growth factor (EGF), insulin-like growth factor (ILGF), vascular endothelial growth factor (VEGF), and platelet-derived growth factor (PDGF).

DOCUMENT-IDENTIFIER: US 20050272132 A1

TITLE: Production of polyketides and other natural products

----- KWIC -----

Detail Description Paragraph - DETX (371):

[0645] Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular, growth factor and cytokine response in injured vessels. Transplantation 55(6):1409-1418.

DOCUMENT-IDENTIFIER: US 20050255089 A1

TITLE: AAV5 nucleic acids

----- KWIC -----

Detail Description Paragraph - DETX (11):

[0046] Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV5 vector can include, but are not limited to the following: nucleic acids encoding secretory and nonsecretory proteins, nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma., interleukins, such as IL-1, IL-1.beta., and ILs-2 through -14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; anit-HIV decoy tar elements; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Another target cell is the lung airway cell, which can be used to administer nucleic acids, such as those coding for the cystic fibrosis transmembrane receptor, which could provide a gene therapeutic treatment for cystic fibrosis. Other target cells include muscle cells where useful nucleic acids, such as those encoding cytokines and growth factors, can be transduced and the protein the nucleic acid encodes can be expressed and secreted to exert its effects on other cells, tissues and organs, such as the liver. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Detail Description Paragraph - DETX (86):

[0120] The present invention provides recombinant vectors based on AAV5. Such vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulfate proteoglycans which is very inefficient with AAV2 based vectors. These vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some examples of this type of treatment include, but are not limited to, the

introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

DOCUMENT-IDENTIFIER: US 20050239131 A1

TITLE: Interactive system for presenting and eliminating
substances

----- KWIC -----

Detail Description Paragraph - DETX (110):

[0146] Biocompatible tissue layers made from plastic materials onto which monodisperse PAMA particles had been adhered or copolymers having PAMA as a basic material are primed with organ-specific pegylated cellular growth factor. This allows a rapid and controlled coating of the organ substitute materials.

DOCUMENT-IDENTIFIER: US 20050235367 A1

TITLE: Regulatory sequences capable of conferring expression
of a heterologous DNA sequence in endothelial cells and
uses thereof

----- KWIC -----

Summary of Invention Paragraph - BSTX (45):

[0045] The endothelial cell-specific regulatory sequences of the invention may also be used in gene therapy to promote angiogenesis to treat diseases such as peripheral vascular disease or coronary artery disease (Isner, Circulation 91 (1995), 2687-2692). For example, the regulatory sequences of the invention can be operatively linked to sequences encoding cellular growth factors which promote angiogenesis, e.g., VEGF, acidic fibroblast growth factor, basic fibroblast growth factor and the like.

DOCUMENT-IDENTIFIER: US 20050233447 A1

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Summary of Invention Paragraph - BSTX (11):

[0010] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) isolating the monocytes from human blood; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Summary of Invention Paragraph - BSTX (12):

[0011] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) providing human monocytes; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Summary of Invention Paragraph - BSTX (17):

[0016] The present invention includes and provides a dedifferentiated, programmable stem cell of human monocytic origin manufactured by a process comprising (a) isolating monocytes from human blood; (b) propagating monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

DOCUMENT-IDENTIFIER: US 20050221483 A1

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Summary of Invention Paragraph - BSTX (11):

[0010] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) isolating the monocytes from human blood; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Summary of Invention Paragraph - BSTX (12):

[0011] The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) providing human monocytes; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Summary of Invention Paragraph - BSTX (17):

[0016] The present invention includes and provides a dedifferentiated, programmable stem cell of human monocytic origin manufactured by a process comprising (a) isolating monocytes from human blood; (b) propagating monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

DOCUMENT-IDENTIFIER: US 20050208660 A1

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Detail Description Paragraph - DETX (63):

[0085] Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

DOCUMENT-IDENTIFIER: US 20050197304 A1

TITLE: Nucleic acid therapy to enhance cartilage repair

----- KWIC -----

Summary of Invention Paragraph - BSTX (24):

[0022] In one embodiment, the naked DNA encodes a bioactive agent selected from the group of cartilage morphogens and factors or peptides which block inhibitory signals preventing the repair or regeneration of cartilage. In a particular embodiment, the agent is a factor selected from the group of cellular growth factors, factors that stimulate chondrogenesis, factors that stimulate migration of stromal cells and factors that stimulate matrix deposition. In a particularly preferred embodiment, the agent is selected from the group of an FGF, a TGF, and a BMP. In an exemplary embodiment, the agent is BMP-2.

Detail Description Paragraph - DETX (4):

[0037] The terms "bioactive agent", "bioactive agent(s)", "bioactive factors" and any variants not specifically listed, may be used herein interchangeably, and as used throughout the present application and claims refer to peptides, compounds or factors which are capable of enhancing or otherwise stimulating the generation, production, regeneration and/or repair of cartilage and will include cartilage morphogens and factors or peptides which block inhibitory signals preventing the repair or regeneration of cartilage. Examples of bioactive factors of use in the present invention include, but are not limited to cellular growth factors (for instance TGF- β), factors that stimulate chondrogenesis (for example bone morphogenetic proteins (BMPs) that promote cartilage formation), factors that stimulate migration of stromal cells, factors that stimulate matrix deposition and osteogenic molecules. Bioactive agent(s) further include anti-inflammatories and immunosuppressants. Bioactive agent(s) include proteins which ordinarily form part of the cartilage extracellular matrix, including for example, collagens, elastic fibers, reticular fibers, glycoproteins or glycosaminoglycans (heparin sulfate, chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate, keratin sulfate), and hyaluronic acid. Factors for use in the invention include FGF, TGF- β , BMPs (including BMP-2, BMP-2B, BMP-7, BMP-11), cartilage oligomeric matrix protein (COMP), IL-10, IL-1 receptor antagonist, latent TGF- β -binding protein (LTBP-3), Smads and GDF-5. Exemplary of a bioactive agent for use in the present invention is BMP-2 as described and demonstrated in the Examples herein, in one embodiment such BMP-2 having the nucleic acid and amino acid sequences as described herein and presented in FIGS. 6 and 7, respectively (SEQ ID NOS: 1 and 2, respectively). The present invention contemplates that bioactive agent(s) include combinations of one or more bioactive agent, particularly and including wherein their activities or capabilities may be complementary or additive. Accordingly, proteins displaying substantially equivalent or altered activity are likewise

contemplated. These modifications may be deliberate, for example, such as modifications obtained through site-directed mutagenesis, or may be accidental, such as those obtained through mutations in hosts that are producers of the complex or its named subunits. Also, the terms "bioactive agent", "bioactive agent(s)", "bioactive factors" and the exemplary "BMP-2" are intended to include within their scope proteins specifically recited herein as well as all substantially homologous analogs and allelic variations.

Detail Description Paragraph - DETX (56):

[0089] In one embodiment, the naked DNA encodes a bioactive agent selected from the group of cartilage morphogens and factors or peptides which block inhibitory signals preventing the repair or regeneration of cartilage. In a particular embodiment, the agent is a factor selected from the group of cellular growth factors, factors that stimulate chondrogenesis, factors that stimulate migration of stromal cells and factors that stimulate matrix deposition. In a particularly preferred embodiment, the agent is selected from the group of an FGF, a TGF, and a BMP. In an exemplary embodiment, the agent is BMP-2.

Claims Text - CLTX (9):

8. The composition of any of claims 1-3 wherein the bioactive agent is a factor selected from the group of cellular growth factors, factors that stimulate chondrogenesis, factors that stimulate migration of stromal cells and factors that stimulate matrix deposition.

Claims Text - CLTX (18):

17. The method of any of claims 11-14 wherein the bioactive agent is a factor selected from the group of cellular growth factors, factors that stimulate chondrogenesis, factors that stimulate migration of stromal cells and factors that stimulate matrix deposition.

DOCUMENT-IDENTIFIER: US 20050180952 A1

TITLE: Methods for intradermal delivery of therapeutics
agents

----- KWIC -----

Detail Description Paragraph - DETX (90):

[0143] The present invention provides methods for administering antineoplastic agents. Such antineoplastic agents include a variety of agents including cytokines, angiogenesis inhibitors, classic anticancer agents and therapeutic antibodies. Cytokines immunomodulating agents and hormones that may be used in accordance with the invention include, but are not limited to interferons, interleukins (IL-1, -2, -4, -6, -8, -12) and cellular growth factors.

DOCUMENT-IDENTIFIER: US 20050176044 A1

TITLE: Polynucleotides and polypeptides encoding receptors

----- KWIC -----

Summary of Invention Paragraph - BSTX (12):

[0013] Moreover, the EGFR family of plasma membrane proteins are an integral component of normal cellular proliferation and in the pathogenesis of the cancerous state. The family is relatively small and includes the EGFR, c-erbB-2, c-erbB-3, and others. Various cancers are correlated with aberrant expression of one or more of these genes. A number of ligands have been identified which bind to the EGFR-like receptors listed above including TGF- α , heparin-binding EGF, amphiregulin, criptoregulin, heregulin, and others. A large fraction of adenocarcinomas examined to date, especially those of the breast, colon, and pancreas, are typified by the amplification or overexpression of the c-erbB-2 gene. EGF, or an analogous ligand, initiates the cellular growth factor response by binding to the EGFR, or EGFR-related, receptor. Following the binding event, the receptor molecule dimerizes activating its intracellular tyrosine kinase domain. This event results in the phosphorylation of specific tyrosine residues near the carboxy terminus of the receptor. The diversity of signals able to be transduced through the relatively small number of EGFR-related receptor molecules is amplified considerably by the recent finding that EGFR-like receptor molecules can function when dimerized with other EGFR family members forming heterodimers.

DOCUMENT-IDENTIFIER: US 20050159396 A1

TITLE: Compositions and methods of treatment for inflammatory diseases

----- KWIC -----

Detail Description Paragraph - DETX (39):

[0050] Antioxidants, such as NAC, and 5-ASA possess the ability to scavenge oxygen free radicals, inhibit inducible NO formation and to down regulate nuclear factor kB (NF-kB) activity (9, 10, 15-17). Furthermore, antioxidants, such as phenyl N-tert-butylnitron, and 5-ASA have been shown to inhibit cytokine production, including tumor necrosis factor TNF.alpha., and to retard adhesion molecule expression and B-cell mediated antibody production (10, 18-20) in experimented models of colitis. Separately and together these agents can, thus, be envisioned to moderate immunocyte (T cell) mediated cytokine elaboration, neutrophil generation of ROS and NO, prostaglandin release and to facilitate an environment for unopposed cellular and growth factor-mediated tissue repair. These results show that treatment with the NAC plus 5-ASA combination cause marked improvement in indices of colitis and, furthermore, demonstrate prominent features of epithelial repair, and mucosal architectural and glandular restoration. These data combined with the near normalization of MPO activity and marked reduction in cytokine (ILa, ILb, IL6) expression indicate that therapy with the NAC plus 5-ASA combination exerts a significantly greater anti-inflammatory and reparative effect in TNBS colitis than either 5-ASA or NAC when used alone.

DOCUMENT-IDENTIFIER: US 20050148078 A1

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Detail Description Paragraph - DETX (63):

[0085] Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, AppAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the omithine transcarbamyase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

DOCUMENT-IDENTIFIER: US 20050148077 A1

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Detail Description Paragraph - DETX (63):

[0085] Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1 , and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

DOCUMENT-IDENTIFIER: US 20050147960 A1

TITLE: In vitro development of tissues and organs

----- KWIC -----

Summary of Invention Paragraph - BSTX (14):

[0012] The scaffold typically supports the multipotent cells. The term "supports" refers to the situation where cells are adherent to the interior and exterior surfaces of the scaffold, and also the situation where the cells are simply resting on the interior and exterior surfaces of the scaffold. Typically, substantially all of the population of multipotent cells will adhere to the surfaces of the scaffold. However, cells undergoing division do not adhere to the surfaces of the scaffold and may simply rest in position. Different scaffold materials may differ in mechanical properties, stabilities (and may be biodegradable), ability to assume a macroscopic shape (e.g., sheet vs spherical), and biocompatibility. Scaffolds may be synthetic, naturally derived or semisynthetic. Polymers include degradable synthetic bulk polymers. These include: 1) synthetic polyesters (including polyesters derived from lactide, glycolide, and caprolactone). Other examples include poly hydroxybutyrate, copolymers of polyhydroxybutyrate with hydroxyvalerate, poly-4 hydroxyputyrate, 2) Synthetic gels (including PEO based substrates), 3) Natural polymers derived from extracellular matrix proteins and derivatives (e.g., collagen) and materials derived from plants and seaweed. Members of this group include type I collagen, laminin family proteins and fibrin. Matrices may be derived from by extraction or partial purification of whole tissue and may contain residual growth factors. Natural polysaccharides are another class which includes hyaluonic acid, alginate. 4) Synthetic materials with tailored biological ligands (examples include the inclusion of fibronectin RGD adhesion recognition sequences and other peptides that promote cellular adhesion, and cellular growth factors and nutrients).

DOCUMENT-IDENTIFIER: US 20050119718 A1

TITLE: Absorbable myocardial lead fixation system

----- KWIC -----

Detail Description Paragraph - DETX (11):

[0030] In another embodiment, the material of the anchor mechanism 44 includes an agent, biologic material or drug, released as the anchor mechanism 44 dissolves, which would alter the local environment of the lead implantation site. This material could be selected to include anti-inflammatory material, angiogenic factors or cellular growth factors or modifiers to enhance healing and low stimulation thresholds.

DOCUMENT-IDENTIFIER: US 20050106560 A1

TITLE: Selection methods

----- KWIC -----

Detail Description Paragraph - DETX (107):

[0200] Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detail Description Paragraph - DETX (111):

[0204] Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

DOCUMENT-IDENTIFIER: US 20050100549 A1

TITLE: Regulation of cytotrophoblast cell differentiation and
cell migration

----- KWIC -----

Abstract Paragraph - ABTX (1):

The present invention is predicated on the discovery of certain interactions between cellular growth factors and opposing actions that control differentiation and migration or invasion of cytotrophoblasts into the uterine endometrium during pregnancy. IGF-II and latent transforming growth factor beta (TGF.beta.), the inactive precursor of TGF.beta., compete for binding to the CIM6P receptor. IGF-II prevents latent TGF.beta. binding to the CIM6P receptor. The invention therefore offers a method of regulating and directing cytotrophoblast differentiation and function based on the interaction between IGF-II, latent TGF.beta. and the CIM6P receptor. There is disclosed a method of regulating cytotrophoblast and stem cell differentiation and migration characterized by adjusting levels of insulin-like growth factor II (IGF-II) available for binding to the cation-independent mannose-6-phosphate (CIM6P) receptor. The discovery may be applied to embryonic or adult stem cells to control their differentiation and migratory behaviour.

Summary of Invention Paragraph - BSTX (16):

[0013] The present invention is predicated on the discovery of certain interactions between cellular growth factors and opposing actions that control differentiation and migration or invasion of cytotrophoblasts into the uterine endometrium which, during pregnancy, is called the decidua. In addition, this discovery may be applied to embryonic or adult stem cells to control their differentiation and migratory behaviour.

DOCUMENT-IDENTIFIER: US 20050069572 A1

TITLE: Multi-layered polymerizing hydrogels for tissue
regeneration

----- KWIC -----

Detail Description Paragraph - DETX (18):

[0107] Optionally, various additives can be included in the hydrogel solution such as 100 U/ml of penicillin and 100 .mu.g/ml streptomycin to inhibit microbacterial contamination. However, these are not the only bioactive additives that can be included in the hydrogel solution. For example, the bioactive additives could include, singly or in combination, growth factors, cell differentiation factors, other cellular mediators, nutrients, antibiotics, antiinflammatories, and other pharmaceuticals. Although not limiting, some suitable cellular growth factors, depending upon the cell type to be encapsulated in either the hydrogel of the same or adjacent hydrogel layer, include heparin binding growth factor (HBGF), transforming growth factor (TGF.alpha. or TGF.beta.), alpha fibroblastic growth factor (FGF), epidermal growth factor (EGF), vascular endothelium growth factor (VEGF), various angiogenic factors, nerve growth factor (NGF) and muscle morphologic growth factor.

DOCUMENT-IDENTIFIER: US 20050065328 A1

TITLE: Gastrokines and derived peptides including inhibitors

----- KWIC -----

Abstract Paragraph - ABTX (1):

A novel group of gastrokines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Control of mammalian gastro-intestinal tissues growth and repair is facilitated by the use of the proteins, making the proteins candidates for therapies.

Summary of Invention Paragraph - BSTX (2):

[0001] A novel group of Gastric Antrum Mucosal Proteins that are gastrokines, is characterized. A member of the gastrokine group is designated AMP-18. AMP-18 genomic DNA, and cDNA molecules are sequenced for human and mouse, and the protein sequences are predicted from the nucleotide sequences. The cDNA molecule for pig AMP-18 is sequenced and confirmed by partial sequencing of the natural protein. The AMP-18 protein and active peptides derived from its sequence are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein sequence. Control of mammalian gastro-intestinal tissues growth and repair is facilitated by the use of the protein or peptides, making the protein and the derived peptides candidates for therapies.

Summary of Invention Paragraph - BSTX (6):

[0004] A novel gene product designated Antrum Mucosal Protein 18 ("AMP-18") is a gastrokine. The protein was discovered in cells of the stomach antrum mucosa by analysis of cDNA clones obtained from humans, pigs, and mice. The protein is a member of a group of cellular growth factors or cytokines, more specifically gastrokines. The AMP-18 cDNA sequences predict a protein 185 amino acids in length for both pig and man. The nucleotide sequences also predict a 20-amino acid N-terminal signal sequence for secreted proteins. The cleavage of this N-terminal peptide from the precursor (preAMP-18) was confirmed for the pig protein; this cleavage yields a secreted protein 165 amino acids in length and ca. 18,000 Daltons (18 kD) in size. Human and mouse genomic DNA sequences were also obtained and sequenced. A human genomic DNA was isolated in 4 overlapping fragments of sizes 1.6 kb, 3 kb, 3.3 kb and 1.1 kb respectively. The mouse genomic DNA sequence was isolated in a single BAC clone.

DOCUMENT-IDENTIFIER: US 20050065152 A1

TITLE: 1-Adamantyl chalcones for the treatment of
proliferative disorders

----- KWIC -----

Detail Description Paragraph - DETX (111):

[0133] The compounds of the present invention were evaluated by comparing breast cancer cell lines MCF-7 (ER-positive) and MDA-MB435 (ER-negative) with noncancerous breast epithelial cells (MCF-10). Those compounds that showed a high level of antiproliferative activity against tested breast cancer cell lines, but not against normal breast epithelial cells were evaluated for in vitro mechanism of action by looking at their effects against cellular growth factors, Epidermal Growth Factor (EGF), and Transforming Growth Factor (TGF-alpha).

DOCUMENT-IDENTIFIER: US 20050059151 A1

TITLE: Compositions and methods for priming monocytic dendritic cells and t cells for th-1response

----- KWIC -----

Detail Description Paragraph - DETX (15):

[0035] Isolated dendritic cell precursors can be cultured ex vivo for differentiation, maturation and/or expansion. (As used herein, isolated immature dendritic cells, dendritic cell precursors, T cells, and other cells, refers to cells that, by human hand, exists apart from their native environment, and are therefore not a product of nature. Isolated cells can exist in purified form, in semi-purified form, or in a non-native environment.) Briefly, ex vivo differentiation typically involves culturing dendritic cell precursors, or populations of cells having dendritic cell precursors, in the presence of one or more differentiation agents. Suitable differentiating agents can be, for example, cellular growth factors (e.g., cytokines such as (GM-CSF), Interleukin 4 (IL-4), Interleukin 13 (IL-13), and/or combinations thereof). In certain embodiments, the monocytic dendritic cells precursors are differentiated to form monocyte-derived immature dendritic cells.

DOCUMENT-IDENTIFIER: US 20050058631 A1

TITLE: Postpartum cells derived from placental tissue, and
methods of making and using the same

----- KWIC -----

Detail Description Paragraph - DETX (238):

[0274] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20050058630 A1

TITLE: Postpartum-derived cells for use in treatment of
disease of the heart and circulatory system

----- KWIC -----

Detail Description Paragraph - DETX (108):

[0150] The invention also provides cell lysates, soluble cell fractions and membrane-enriched cell fractions prepared from the populations of the postpartum cells. Such lysates and fractions have many utilities. Use of cell lysates, and more particularly soluble cell fractions, in vivo allows the beneficial intracellular milieu to be used in a patient allogeneic patient without stimulating allogeneic lymphocytes, or generating other adverse immunological responses, or triggering rejection. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their Growth Medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or another solution. For making lysates from cells directly in the growth medium it is preferred that cells are grown in serum from the species in which the lysates are to be used, in some embodiments, washed cells may be preferred. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, enriched, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or, for example, with syngeneic or autologous live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example, needed cellular growth factors to a patient. Preferably, the lysates are not immunogenic, and more preferably they are immunologically tolerated in a broad population of syngeneic and allogeneic recipients without adverse immunological consequences or reaction. Cell lysates of the invention are useful from cells at any stage or age which have been grown under conditions for growth and expansion, for example on Growth Medium. Even senescent cells are useful for the preparation of lysate and can provide certain factors which are biologically useful. Nonviable or even dead or killed cells have utility for preparing lysates, and cellular fractions. Also useful are lysates from cells which have been exposed to factors which tend to induce them along a mesenchymal pathway, particularly towards cardiomyogenic, angiogenic, hemangiogenic, and vasculogenic lines. Cell lysates from differentiated cells, or cells more committed than the PPDCs are also desirable. For example, lysates from cells with characteristics of cardiomyoblasts, cardiomyocytes, angioblasts, hemangioblasts and the like, or

their progenitors are also useful and contemplated for use herewith.

DOCUMENT-IDENTIFIER: US 20050058629 A1

TITLE: Soft tissue repair and regeneration using
postpartum-derived cells

----- KWIC -----

Detail Description Paragraph - DETX (269):

[0300] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20050055010 A1

TITLE: Method for altering insulin pharmacokinetics

----- KWIC -----

Detail Description Paragraph - DETX (13):

[0063] The present invention provides methods for administering antineoplastic agents. Such antineoplastic agents include a variety of agents including cytokines, angiogenesis inhibitors, classic anticancer agents and therapeutic antibodies. Cytokines immunomodulating agents and hormones that may be used in accordance with the invention include, but are not limited to interferons, interleukins (IL-1, -2, -4, -6, -8, -12) and cellular growth factors.

DOCUMENT-IDENTIFIER: US 20050054564 A1

TITLE: Control of growth and repair of gastro-intestinal
tissues by gastrokinines and inhibitors

----- KWIC -----

Abstract Paragraph - ABTX (1):

A novel group of gastrokinines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Cytoprotection and control of mammalian gastro-intestinal tissue growth and repair (restitution) is facilitated by the use of the proteins, making the proteins candidates for therapies in inflammatory bowel disease and gastric ulcers.

Summary of Invention Paragraph - BSTX (2):

[0002] A novel group of Gastric Antrum Mucosal Proteins that are gastrokinines, is characterized. A member of the gastrokine group is designated AMP-18. AMP-18 genomic DNA, and cDNA molecules are sequenced for human and mouse, and the protein sequences are predicted from the nucleotide sequences. The cDNA molecule for pig AMP-18 is sequenced and confirmed by partial sequencing of the natural protein. The AMP-18 protein and active peptides derived from its sequence are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein sequence. Control of mammalian gastro-intestinal tissues growth and repair is facilitated by the use of the protein or peptides, making the protein and the derived peptides candidates for therapies.

Summary of Invention Paragraph - BSTX (6):

[0005] A novel gene product designated Antrum Mucosal Protein 18 ("AMP-18") is a gastrokine. The protein was discovered in cells of the stomach antrum mucosa by analysis of cDNA clones obtained from humans, pigs, and mice. The protein is a member of a group of cellular growth factors or cytokines, more specifically gastrokinines. The AMP-18 cDNA sequences predict a protein 185 amino acids in length for both pig and man. The nucleotide sequences also predict a 20-amino acid N-terminal signal sequence for secreted proteins. The cleavage of this N-terminal peptide from the precursor (preAMP-18) was confirmed for the pig protein; this cleavage yields a secreted protein 165 amino acids in length and ca. 18,000 Daltons (18 kD) in size. Human and mouse genomic DNA sequences were also obtained and sequenced. A human genomic DNA was isolated in 4 overlapping fragments of sizes 1.6 kb, 3 kb, 3.3 kb and 10.1 kb respectively. The mouse genomic DNA sequence was isolated in a single BAC clone.

DOCUMENT-IDENTIFIER: US 20050053642 A1

TITLE: Biocompatible materials

----- KWIC -----

Detail Description Paragraph - DETX (446):

[0564] A first determinant as defined herein comprises a biologically active compound comprising a polypeptide, or a part thereof, a nucleic acid moiety, a carbohydrate moiety, and a lipid moiety, including any combination thereof. The biologically active compound is preferably selected from the group consisting of membrane associated and/or extracellular matrix polypeptides natively produced by a microbial cell, a plant cell or a mammalian cell. The biologically active compound in another embodiment is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

Detail Description Paragraph - DETX (523):

[0641] According to the method for producing the material according to the invention, said method may comprising the further step of contacting said material with a first determinant comprising a biologically active compound. The biologically active compound is preferably a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, or an antagonist to a receptor. The biologically active compound may be membrane associated and/or an extracellular matrix polypeptide natively produced by a microbial cell, a plant cell or a mammalian cell.

Claims Text - CLTX (77):

77. Material according to claim 74 wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

Claims Text - CLTX (118):

137. Method according to claim 136, wherein said biologically active compound is selected from the group consisting of a polypeptide, an antibody, a polyclonal antibody, a monoclonal antibody, an immunogenic determinant, an antigenic determinant, a receptor, a receptor binding protein, an interleukine, a cytokine, a cellular differentiation factor, a cellular growth factor, and an antagonist to a receptor.

DOCUMENT-IDENTIFIER: US 20050048645 A1

TITLE: Method of treating or preventing disease characterized
by cryptococcus neoformans infection

----- KWIC -----

Detail Description Paragraph - DETX (7):

[0019] A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art (i.e., the well-known technique of ex vivo culture of peripheral blood mononuclear cells in IL-4 and GM-CSF [and/or other cytokines] to yield antigen-presenting cells). Briefly, ex vivo culture and expansion comprises: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as FL, IL-1, IL-3 and c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20050037491 A1

TITLE: Repair and regeneration of ocular tissue using
postpartum-derived cells

----- KWIC -----

Detail Description Paragraph - DETX (63):

[0091] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20050037330 A1

TITLE: Composition for maintaining organ and cell viability

----- KWIC -----

Summary of Invention Paragraph - BSTX (14):

[0012] b) the nanoparticles of the second phase comprise one or more of the following: lipids, fatty acids, sterols, free fatty acids, optional cellular growth factors; and

Detail Description Paragraph - DETX (28):

[0043] In another preferred embodiment, the second phase also includes hydrophilic supportive endocrine factors such as hydrocortisone, thyroxine or its derivatives, and the like. Further supportive components can include, for example, cellular growth factors, e.g., epithelial and endothelial growth factors, including physiologically compatible amounts of vascular endothelial growth factor, platelet derived endothelial growth factor, epithelial growth factor, hepatocyte growth factor, platelet derived endothelial growth factor, and the like. Optionally, other factors contemplated to be included in the second phase include intercellular messengers such as prostoglandins, e.g., prostaglandin E1. Preferably, physiologically compatible surfactants and detergents are also included, e.g., one or more water-soluble surfactants, preferably an amphiphilic block copolymer with a molecular weight of several thousand Daltons, such as a polypropyleneoxide-polyethyleneoxide block copolymer surfactant (e.g., Pluronic F-68; from BASF) and/or nonionic surfactants. Suitable nonionic surfactants include, e.g., polyoxyethylene derivatives of sorbitol esters, e.g., polyoxyethylene sorbitan monooleate surfactants that are commercially available as TWEEN.RTM. (Atlas Chemical Co.). TWEEN 80.RTM. is particularly preferred. The core portion of the two-phase compositions of the invention preferably do not include a pharmaceutically significant quantity of a phosphatidic acid or sugar, or a lysophosphotidic acid or sugar.

Claims Text - CLTX (7):

6. The two-phase composition of claim 1, further comprising cellular growth factors.

Claims Text - CLTX (8):

7. The two-phase composition of claim 6, wherein said cellular growth factors are selected from the group consisting of epithelial and endothelial growth factors, vascular endothelial growth factors, platelet derived endothelial growth factors, epithelial growth factors, hepatocyte growth factors, and mixtures thereof. The two-phase composition of claim 1 that is Formula-I.

DOCUMENT-IDENTIFIER: US 20050032209 A1

TITLE: Regeneration and repair of neural tissue using
postpartum-derived cells

----- KWIC -----

Detail Description Paragraph - DETX (65):

[0092] Cell lysates or cell soluble fractions prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically-acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates or fractions thereof may be used in vitro or in vivo, alone or for example, with autologous or syngeneic live cells. The lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20050031582 A1

TITLE: Control of growth and repair of gastro-intestinal
tissues by gastrokinines and inhibitors

----- KWIC -----

Abstract Paragraph - ABTX (1):

A novel group of gastrokinines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Cytoprotection and control of mammalian gastro-intestinal tissue growth and repair (restitution) is facilitated by the use of the proteins, making the proteins candidates for therapies in inflammatory bowel disease, mucositis, and gastric ulcers.

Summary of Invention Paragraph - BSTX (5):

[0004] A novel group of Gastric Antrum Mucosal Proteins that are gastrokinines, is characterized. A member of the gastrokine group is designated AMP-18. AMP-18 genomic DNA, and cDNA molecules was sequenced for human and mouse, and the protein sequences are predicted from the nucleotide sequences. The cDNA molecule for pig AMP-18 was sequenced and confirmed by partial sequencing of the natural protein. The AMP-18 protein and active peptides derived from its sequence are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, were also derived from the AMP-18 protein sequence. Control of mammalian gastro-intestinal tissues growth and repair was facilitated by the use of the protein or peptides, making the protein and the derived peptides candidates for therapies.

Summary of Invention Paragraph - BSTX (6):

[0005] The protein was discovered in cells of the stomach antrum mucosa by analysis of cDNA clones obtained from humans, pigs, and mice. The protein is a member of a group of cellular growth factors or cytokines, more specifically gastrokinines. The AMP-18 cDNA sequences predict a protein 185 amino acids in length for both pig and man. The nucleotide sequences also predict a 20-amino acid N-terminal signal sequence for secreted proteins. The cleavage of this N-terminal peptide from the precursor (preAMP-18) was confirmed for the pig protein; this cleavage yields a secreted protein 165 amino acids in length and ca. 18,000 Daltons (18 kD) in size. Human and mouse genomic DNA sequences were also obtained and sequenced. A human genomic DNA was isolated in 4 overlapping fragments of sizes 1.6 kb, 3 kb, 3.3 kb and 1.1 kb respectively. The mouse genomic DNA sequence was isolated in a single BAC clone.

DOCUMENT-IDENTIFIER: US 20050019865 A1

TITLE: Cartilage and bone repair and regeneration using
postpartum-derived cells

----- KWIC -----

Detail Description Paragraph - DETX (250):

[0283] Cell lysates prepared from the populations of the postpartum-derived cells also have many utilities. In one embodiment, whole cell lysates are prepared, e.g., by disrupting cells without subsequent separation of cell fractions. In another embodiment, a cell membrane fraction is separated from a soluble fraction of the cells by routine methods known in the art, e.g., centrifugation, filtration, or similar methods. Use of soluble cell fractions in vivo allows the beneficial intracellular milieu to be used in a patient without triggering rejection or an adverse response. Methods of lysing cells are well-known in the art and include various means of mechanical disruption, enzymatic disruption, or chemical disruption, or combinations thereof. Such cell lysates may be prepared from cells directly in their growth medium and thus containing secreted growth factors and the like, or may be prepared from cells washed free of medium in, for example, PBS or other solution. Washed cells may be resuspended at concentrations greater than the original population density if preferred. Cell lysates prepared from populations of postpartum-derived cells may be used as is, further concentrated, by for example, ultrafiltration or lyophilization, or even dried, partially purified, combined with pharmaceutically acceptable carriers or diluents as are known in the art, or combined with other compounds such as biologicals, for example pharmaceutically useful protein compositions. Cell lysates may be used in vitro or in vivo, alone or for example, with cells. The cell lysates, if introduced in vivo, may be introduced locally at a site of treatment, or remotely to provide, for example needed cellular growth factors to a patient.

DOCUMENT-IDENTIFIER: US 20050003388 A1

TITLE: Calcium independent phospholipase A2 ϵ
polynucleotides and polypeptides and methods therefor

----- KWIC -----

Summary of Invention Paragraph - BSTX (6):

[0005] The function of complex living biological organisms relies on the meticulous control of cellular activity, including close regulation of cell growth, proliferation and function. The family of enzymes known as the phospholipases A₂ has been implicated in the control of cellular activity by catalyzing the esterolytic cleavage of fatty acids from phospholipids, thereby regulating the release of lipid second messengers, cellular growth factors, and the properties of the cellular membrane (Samuelsson et al., Annu. Rev. Biochem. 47:997-1029, 1978; Moolenaar, W. H., Curr. Opin. Cell. Biol. 7:203-10, 1995). In particular, by controlling the production of second messengers such as arachidonic acid and its biologically active eicosanoid metabolites, phospholipases A₂ are involved in modulating such processes as cellular growth programs, inflammation, vascular tone and ion channel function. (Needleman et al., Annu. Rev. Biochem. 55:69-102, 1986).

DOCUMENT-IDENTIFIER: US 20040248320 A1

TITLE: Medical device with array of electrode-containing
reservoirs

----- KWIC -----

Detail Description Paragraph - DETX (24):

[0048] A wide variety of molecules can be contained in and released from the microchip devices. Examples of the molecules include drugs, diagnostic reagents, fragrances, dyes or coloring agents, sweeteners and other flavoring agents, and compounds used in tissue culture, such as cellular growth factors.

DOCUMENT-IDENTIFIER: US 20040247663 A1

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Summary of Invention Paragraph - BSTX (4):

[0003] A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments for use in active immunity, cytokines and cellular growth factors for stimulating immunological inflammatory responses, hormones, and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, N. V., et al., Proc. Natl. Acad. Sci. USA 84:1487-1491 (1987); Philips, M. L., et al., Science 250:1130-1132 (1990); Waldmann, T. A., Annu. Rev. Immunol. 10:675-704 (1992)).

Summary of Invention Paragraph - BSTX (14):

[0012] (c) a cytokine or a cellular growth factor, for use in stimulating an immune response in the subject;

Claims Text - CLTX (3):

2. The composition of claim 1, wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (9):

8. The composition of claim 7 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (15):

14. The composition of claim 13 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (21):

20. The composition of claim 19 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1

inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (27):

26. The composition of claim 25 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (33):

32. The composition of claim 31 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (39):

38. The composition of claim 37 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (45):

44. The composition of claim 43 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

DOCUMENT-IDENTIFIER: US 20040247563 A1

TITLE: Method of enhancing lymphocyte-mediated immune responses

----- KWIC -----

Detail Description Paragraph - DETX (63):

[0081] Those of skill in the art will also recognize that various ex vivo culture techniques can also be employed in the present invention. A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. U.S. Pat. No. 6,017,527 describes a method of culturing and activating DC; other suitable methods are known in the art. In one aspect of the invention, ex vivo culture and expansion comprises: (1) collecting CD34+hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as Flt3L, IL-1, IL-3, RANKL and c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20040203143 A1

TITLE: Generation of dendritic cells from monocytic dendritic precursor cells with GM-CSF in the absence of additional cytokines

----- KWIC -----

Summary of Invention Paragraph - BSTX (9):

[0009] Subsequent to essentially all of the reported methods for the preparation of a cell population enriched for dendritic cell precursors, the cell populations are typically cultured ex vivo or in vitro for differentiation of the dendritic cell precursors or maintenance, and/or expansion of the dendritic cells. Briefly, ex vivo differentiation of monocytic dendritic cell precursors has involved culturing the mixed cell populations enriched for dendritic cell precursors in the presence of combinations of cellular growth factors, such as cytokines. For example, monocytic dendritic cell precursors require granulocyte/monocyte colony-stimulating factor (GM-CSF) in combination with at least one other cytokine selected from, for example, either Interleukin 4 (IL-4), Interleukin 15 (IL-15), Interleukin 13 (IL-13), interferon .alpha. (IFN-.alpha.), and the like, to differentiate the cells into an optimal state for antigen uptake, processing, and/or presentation. The numbers of dendritic cells from non-monocytic dendritic cell precursors, such as those obtained by removal of monocytes and other non-dendritic precursor cells (adsorption to a plastic surface) or selection for CD34.sup.+ cells, have also been expanded by culture in the presence of certain cytokines. Either GM-CSF alone or a combination of GM-CSF and IL-4 have been used in methods to produce dendritic cell populations from such proliferating dendritic cell precursors for therapeutic use.

DOCUMENT-IDENTIFIER: US 20040197905 A1

TITLE: Methods and devices for monitoring cellular metabolism
in microfluidic cell-retaining chambers

----- KWIC -----

Detail Description Paragraph - DETX (9):

[0038] Low reagent consumption may be especially important when precious or rare reagents are used, particularly when the effect of purified cellular growth factors are being tested on cells. Low reagent consumption may also be important when drug candidates from chemical microlibraries are being tested on cells. A large synthetic effort may be required to create even small amounts of each reagent in such microlibraries because they may include a very large number of compounds, e.g., one-thousand to one-million compounds, or more.

DOCUMENT-IDENTIFIER: US 20040197903 A1

TITLE: Method for induction of proliferation of natural
killer cells by dendritic cells cultured with GM-CSF
and IL-15

----- KWIC -----

Summary of Invention Paragraph - BSTX (9):

[0008] Subsequent to essentially all of the reported methods for the preparation of a cell population enriched for dendritic cells, the cell populations are typically cultured ex vivo for differentiation and/or expansion of the dendritic cells. Briefly, ex vivo differentiation typically has involved culturing the mixed cell populations enriched for dendritic cells in the presence of cellular growth factors, such as cytokines. For example, granulocyte/monocyte colony-stimulating factor (GM-CSF) and interleukin 4 (IL-4), Interleukin 7 (IL-7), or Interleukin 13 (IL-13), and the like, have been used to support and/or differentiate dendritic cells. The numbers of dendritic cells have also been expanded by culture in the presence of cytokines.

DOCUMENT-IDENTIFIER: US 20040186052 A1

TITLE: Cytomodulating peptides and methods for treating
neurological disorders

----- KWIC -----

Detail Description Paragraph - DETX (13):

[0076] Parkinson's disease is a chronic neurodegenerative disease characterized by the progressive loss of tyrosine hydroxylase(TH)-express- ing dopaminergic neurons of the substantia nigra. Symptoms of Parkinson's disease include tremor, rigidity and bradykinesia. In advanced stages, patients exhibit problems with speech and a decline in cognitive function. A number of cellular and growth factor therapies have been tested with varied results. For example, see Dauer et al., Neuron, 39:889-909, 2003. Direct infusion of GDNF into the putamen was recently reported to improve patients' performance (Gill et al., Nat. Med., 9:589-595, 2003). In addition, the JNK inhibitor "CEP-1347" is currently in Phase II clinical trials for the treatment of Parkinson's disease.

DOCUMENT-IDENTIFIER: US 20040185519 A1

TITLE: Calcium-independent phospholipase A2 induces ischemic
ventricular arrhythmias and decreases infarction size

----- KWIC -----

Detail Description Paragraph - DETX (71):

[0085] The function of complex biological organisms relies on the meticulous control of cellular activity, including close regulation of cell growth, proliferation and function. The family of enzymes known as the phospholipases A.sub.2 has been implicated in the control of cellular activity by catalyzing the esterolytic cleavage of fatty acids from phospholipids, thereby regulating the release of lipid second messengers, cellular growth factors, and the properties of the cellular membrane (Samuelsson et al., Annu. Rev. Biochem. 47:997-1029, 1978; Moolenaar, W. H., Curr. Opin. Cell. Biol. 7:203-10, 1995). In particular, by controlling the production of second messengers such as arachidonic acid and its biologically active eicosanoid metabolites, the phospholipases A.sub.2 are involved in modulating such processes as cellular growth programs, inflammation, vascular tone and ion channel function. (Needleman et al., Annu. Rev. Biochem. 55:69-102, 1986).

DOCUMENT-IDENTIFIER: US 20040175364 A1

TITLE: Gene transfer with adenoviruses having modified fiber proteins

----- KWIC -----

Detail Description Paragraph - DETX (8):

[0027] DNA sequences encoding therapeutic agents include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding G-CSF, GM-CSF, TGF-.alpha., TGF-.beta., and fibroblast growth factor; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; genes encoding co-stimulatory antigens, such as B7.1; genes encoding chemotactic agents, such as lymphotactin, the cystic fibrosis transmembrane conductance regulator (CFTR) genes; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuMn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; genes encoding anti-angiogenic factors, such as, for example, endothelial monocyte activating polypeptide-2 (EMAP-2); the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; cell cycle control agent genes, such as, for example, the p21 gene; antisense polynucleotides to the cyclin G1 and cyclin D1 genes; the endothelial nitric oxide synthetase (ENOS) gene; monoclonal antibodies specific to epitopes contained within the , .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; the dihydrofolate reductase (DHFR) gene; DNA sequences encoding ribozymes;

antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

DOCUMENT-IDENTIFIER: US 20040156848 A1

TITLE: Therapeutic uses of factors which inhibit or
neutralize MIF activity

----- KWIC -----

Summary of Invention Paragraph - BSTX (10):

[0008] In a specific embodiment of the invention, therapeutic compositions comprising neutralizing MIF monoclonal antibodies are used to treat B and T cell lymphomas. The invention is based, in part, on the Applicants' unexpected finding that MIF is required for the proliferation of T cells in vitro. Neutralizing monoclonal antibodies (mAbs) against MIF directly inhibited the proliferation of anti-CD3 induced primary T cells. These results suggest that MIF functions as a cellular growth factor and that MIF plays a role in regulating cellular proliferation.

DOCUMENT-IDENTIFIER: US 20040143236 A1

TITLE: Thermally-activated reservoir devices

----- KWIC -----

Summary of Invention Paragraph - BSTX (11):

[0010] The reservoirs can contain multiple drugs or other molecules in variable dosages. Each of the reservoirs of a single microchip can contain different molecules and/or different amounts and concentrations, which can be released independently. Examples of molecules to be delivered include drugs, fragrances, dyes or coloring agents, sweeteners, diagnostic reagents, and compounds used in tissue culture, such as cellular growth factors.

DOCUMENT-IDENTIFIER: US 20040142037 A1

TITLE: Lactoferrin compositions and methods of wound treatment

----- KWIC -----

Summary of Invention Paragraph - BSTX (4):

[0003] Relatively few biotechnology products have been developed for treating wounds, such as partial-thickness burns. Most of the efforts have been directed towards chronic wounds, which do require a proper level of cellular growth factors for healing. The most conventional option of chronic ulcer treatment involves sharp debridement to remove all non-viable tissue, a non-weight-bearing regimen, moist saline dressings changed twice daily at which times the skin around the ulcer are cleansed with mild soap and water. Current advanced treatment for chronic ulcers include growth factors, skin replacement therapy, enzymatic and mechanical debridement to clean ischemic tissue, moist wound dressings, non-antibiotic cleansers, antibiotics (Edmonds et al., 2000, Lipsky and Berendt 2000, Moulin et al., 1998, Mandracchia et al., 2001). However, current therapy for chronic wounds is not completely effective. In fact, Regranex.TM. gel or Becaplermin (recombinant-human platelet-derived growth factor-BB), the only biological product in the market for chronic wounds (diabetic neuropathic ulcers) has shown only 9-23% improvement over placebo and 4-22% improvement over good ulcer care alone (Mandracchia et al., 2001, Edmonds et al., 2000, Wieman 1998). Thus, an effective treatment for wounds, chronic and/or acute, is needed.

Detail Description Paragraph - DETX (68):

[0105] A wound is also further defined as a chronic wound. Examples of chronic wounds or chronic ulcers include, but are not limited to diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Yet further, chronic wounds can also include infected wounds. Chronic wounds are wounds that do not repair or do so extremely slowly, and show partial or total lack of structural organization and functional coordination with normal tissue. Chronic wounds or chronic ulcers can be broadly classified into three major types: diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Diabetic ulcers often occur on a foot. Chronic diabetic state and poor glucose control results in poor peripheral circulation and microcirculation due to progressive arteriosclerosis; neuropathic changes that result in an insensate extremity prone to trauma; and intrinsic defects in the wound healing process that may include reduced abundance and response to cellular growth factors. In the case of venous ulcers, venous hypertension causes disturbed microcirculation and pathological changes of the capillaries, elevated persistent levels of pro-inflammatory cytokines and proteases. Fibroblast senesce and respond less to growth factors, which distribute unfavorably. Proteolytic enzymes and their inhibitors are imbalanced. Pressure ulcers occur when skin is under pressure without movement to allow blood flow for 8-12

hours.

DOCUMENT-IDENTIFIER: US 20040137618 A1

TITLE: Decellularized vascular prostheses resistant to
thrombus occlusion and immunological rejection

----- KWIC -----

Summary of Invention Paragraph - BSTX (32):

[0030] It is also an object of the present invention to provide a method of linking decellularized vascular tissue with at least one anti-thrombogenic agent and applying a second linking of at least one cellular growth factor so that the modified vascular tissue may be used as a vascular prosthesis.

DOCUMENT-IDENTIFIER: US 20040131587 A1

TITLE: Method for treatment of tumors using combination
therapy

----- KWIC -----

Detail Description Paragraph - DETX (68):

[0088] Those of skill in the art will also recognize that various ex vivo culture techniques can also be employed in the present invention. A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. U.S. Pat. No. 6,017,527 describes a method of culturing and activating DC; other suitable methods are known in the art. In one aspect of the invention, ex vivo culture and expansion comprises: (1) collecting CD34+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as Flt3L, IL-1, IL-3, RANKL and c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20040121950 A1

TITLE: Drug comprising synthetic peptide analogs for the treatment of cancer

----- KWIC -----

Summary of Invention Paragraph - BSTX (11):

[0009] The receptor tyrosine kinases (RTK) are transactivated by G protein coupled receptors (GPCR). Platelet derived growth factor (PDGF), epidermal growth factor (EGF) and insulin like growth factor 1 (IGF1) are tyrosine phosphorylated subsequent to GPCR activation. The phosphorylated growth factors in turn recruit multiple accessory proteins to activate the mitogen activated protein kinases (MAPK). Human adenocarcinomas have increased constitutive MAPK activity (Ostrowski et al, Br. J Cancer Vol 78, 1301-1306, 1997), and the blockade of this protein kinase suppresses tumour growth in vitro and in vivo (Sebolt-Leopold et al, Nature Medicine, Vol 5, 810-816, 1999). The MAP Kinase pathway is a crucial convergence point for many cytoplasmic signaling networks. MAP kinases form a family of Ser/Thr kinases, which can be activated by cellular growth factors. MAP Kinase lies downstream of the Ras-Raf oncogenic pathway and its activation leads to phosphorylation of nuclear transcription factors resulting in cell proliferation (Ostrowski et al., Br. J Cancer Vol 78, 1301-1306, 1997).

DOCUMENT-IDENTIFIER: US 20040101962 A1

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Claims Text - CLTX (1):

1. Process for the production of dedifferentiated, programmable stem cells of human monocytic origin, characterised in that a) monocytes are isolated from human blood; b) the monocytes are propagated in a suitable culture medium, which contains the cellular growth factor M-CSF; c) the monocytes are cultivated simultaneously with or subsequently to step b) in a culture medium containing IL-3; and d) the human adult dedifferentiated programmable stem cells are obtained by separating the cells from culture medium.

DOCUMENT-IDENTIFIER: US 20040086490 A1

TITLE: AAV4 vector and uses thereof

----- KWIC -----

Detail Description Paragraph - DETX (8):

[0037] Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV4 vector can include, but are not limited to the following: nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; interleukins, such as IL-1, IL-1.beta., and ILs-2 through -14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Detail Description Paragraph - DETX (54):

[0082] The present invention provides recombinant vectors based on AAV4. Such vectors may be useful for transducing erythroid progenitor cells which is very inefficient with AAV2 based vectors. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some examples of this type of treatment include, but are not limited to, the introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

DOCUMENT-IDENTIFIER: US 20040086485 A1

TITLE: Chemeric viral vectors for gene therapy

----- KWIC -----

Summary of Invention Paragraph - BSTX (74):

[0070] DNA sequences encoding therapeutic agents which may be contained in the vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF_α; genes encoding interferons such as Interferon-_α, Interferon-_β, and Interferon-_γ; genes encoding interleukins such as IL-1, IL-1_α, and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.sub.--1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the _β-globin gene; the _α-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-₁ protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the _α-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; DNA sequences encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotension converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

DOCUMENT-IDENTIFIER: US 20040053306 A1

TITLE: Polynucleotides encoding short polypeptides,
polypeptides encoded thereby, and methods of use
thereof

----- KWIC -----

Detail Description Paragraph - DETX (106):

[0177] In many embodiments, a subject secreted protein has one or more of the following activities: (1) functions as a cellular differentiation factor; (2) affects an immune response; (3) functions as a cellular growth factor; (4) functions as a hormone; (5) modulates appetite; (6) affects an endocrine function; (7) functions as a cytokine; (8) functions as a chemokine; (9) functions as a cytotoxic factor; (10) functions to modulate angiogenesis; (11) functions as a vasodilator; (12) functions as a vasoconstrictor; (13) functions to modulate blood pressure; (14) functions to induce cell motility (e.g., chemoattractants).

DOCUMENT-IDENTIFIER: US 20040043962 A1

TITLE: Method for enhancing the effectiveness of cancer
therapies

----- KWIC -----

Summary of Invention Paragraph - BSTX (7):

[0006] Galectin-1 is a highly conserved homodimer of 14-15 kD and is one of the most abundant of the galectins. It binds to laminin which has been found to exert strong regulatory effects on cellular interactions such as adhesion, proliferation, migration and differentiation. In this regard, galectin-1 has been found to strongly influence these processes in various cells. It is believed to be implicated in the secretion of a number of cellular growth factors and interleucins. Galectin-1 has been found to be expressed at very high levels in many cancer cells and is strongly implicated in metastasis.

DOCUMENT-IDENTIFIER: US 20040037845 A1

TITLE: Use of flt3-ligand in the treatment of infection

----- KWIC -----

Summary of Invention Paragraph - BSTX (40):

[0037] The procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Briefly, the term means a method comprising: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-ligand, IL-1, IL-3, c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20040023925 A1

TITLE: Method for enhancing the effectiveness of therapies of
hyperproliferative diseases

----- KWIC -----

Summary of Invention Paragraph - BSTX (4):

[0004] Galectin-1 is a highly conserved homodimer of 14-15 kD and is one of the most abundant of the galectins. It binds to laminin which has been found to exert strong regulatory effects on cellular interactions such as adhesion, proliferation, migration and differentiation. In this regard, galectin-1 has been found to strongly influence these processes in various cells. It is believed to be implicated in the secretion of a number of cellular growth factors and interleukins. Galectin-1 has been found to be expressed at very high levels in many cancer cells and is strongly implicated in metastasis.

DOCUMENT-IDENTIFIER: US 20020055131 A1

TITLE: Uses of thioredoxin

----- KWIC -----

Detail Description Paragraph - DETX (94):

[0155] 4.6.2 Role of Oxidative Inactivation of Thioredoxin as a Cellular Growth Factor

DOCUMENT-IDENTIFIER: US 20020039729 A1

TITLE: Methods & compositions for identifying a protease

----- KWIC -----

Detail Description Paragraph - DETX (25):

[0041] One type of inhibitory protein binds to a receptor on the target cell. This type of inhibitory protein thus may include, but is not limited to, a single-chain antibody fragment to a hapten (Russell et al., Nucleic Acids Research 21 (5), 1081-1085, 1993), CD3 or colonic carcinoma cell antigens (Ager et al., Human Gene Therapy 7 (17), 2157-2164, 1996), or a cellular growth factors such as epidermal growth factor (EGF, Cosset et al., Journal of Virology 69 (10), 6314-6322, 1995), stem cell factor (SCF, Fielding et al., Blood 91 (5), 1802-9, 1998), and insulin-like growth factor I (IGF-I, Chadwick et al., J Mol Biol 285 (2), 485-94, 1999).

DOCUMENT-IDENTIFIER: US 20020034517 A1

TITLE: DENDRITIC CELL STIMULATORY FACTOR

----- KWIC -----

Summary of Invention Paragraph - BSTX (28):

[0024] The procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Briefly, the term means a method comprising: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo . In addition to the cellular growth factors described in U.S. Pat. 5,199,942, other factors such as flt3-ligand, IL-1, IL-3, c-kit ligand, can be used.

DOCUMENT-IDENTIFIER: US 20020028201 A1

TITLE: INTERACTIVE SYSTEM FOR PRESENTING AND ELIMINATING
SUBSTANCES

----- KWIC -----

Detail Description Paragraph - DETX (113):

[0148] Biocompatible tissue layers made from plastic materials onto which monodisperse PAMA particles had been adhered or copolymers having PAMA as a basic material are primed with organ-specific pegylated cellular growth factor. This allows a rapid and controlled coating of the organ substitute materials. Fields of application: liver substitute, bone marrow substitute, lung tissue substitute etc.

DOCUMENT-IDENTIFIER: US 20020012997 A1

TITLE: Lipid vesicles containing adeno-associated virus Rep
protein for transgene integration and gene therapy

----- KWIC -----

Detail Description Paragraph - DETX (13):

[0037] DNA sequences encoding therapeutic agents which may be placed into the genetic construct include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha., interferons, such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1-B, and Interleukins 2 through 14; gene encoding GM-CSF; genes encoding adenosine deaminase or ADA; genes encoding cellular growth factors or cytokines, such as epithelial growth factor (EGF), keratinocyte growth factor (KGF), and lymphokines, which are growth factors for lymphocytes; gene encoding soluble CD4; Factor VII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI, and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; superoxide dismutase genes, such as Cu-SOD, Mn-SOD, and Zn-SOD; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus. Additional therapeutic agents include genetic transcripts such as a messenger RNA, antisense RNA, or ribozymes. It is to be understood, however, that the scope of the present invention is not intended to be limited to the specific therapeutic agents described hereinabove.

DOCUMENT-IDENTIFIER: US 20020009715 A1

TITLE: Methods and compositions for identifying a
polynucleotide encoding a protease

----- KWIC -----

Detail Description Paragraph - DETX (24):

[0041] One type of inhibitory protein binds to a receptor on the target cell. This type of inhibitory protein thus may include, but is not limited to, a single-chain antibody fragment to a hapten (Russell et al., Nucleic Acids Research 21(5), 1081-1085, 1993), CD3 or colonic carcinoma cell antigens (Ager et al., Human Gene Therapy 7(17), 2157-2164, 1996), or a cellular growth factors such as epidermal growth factor (EGF, Cosset et al., Journal of Virology 69(10), 6314-6322, 1995), stem cell factor (SCF, Fielding et al., Blood 91(5), 1802-9, 1998), and insulin-like growth factor I (IGF-I, Chadwick et al., J Mol Biol 285(2), 485-94, 1999).

DOCUMENT-IDENTIFIER: US 20010053523 A1

TITLE: Method for identification of biologically active
peptides and nucleic acids

----- KWIC -----

Detail Description Paragraph - DETX (8):

[0021] Since the efficiency of the non-viral methods commonly used for stable gene transfer into mammalian cells is very low, it would not be possible to establish a peptide expression library in mammalian cells by such methods. In addition non-viral methods generally lead to multiple integrations of DNA in the cell genome in disagreement with the "one cell one ribonucleic acid or peptide" concept. In order to achieve the necessary high efficiency single gene copy transfer a viral vector must be used. Very recently cDNA expression libraries which were constructed using retroviral vectors have been described. From such libraries cytokines and cellular growth factors have been isolated (A. J. M. Murphy et al., Proc. Natl. Acad. Sci. USA, 84, 8277-8281, 1987., B. Y. Wong et al., J. Virol., 68, 5523-31, 1994., J. R. Rayner et al., Mol. Cell. Biol., 14, 880-887, 1994). Expression of well defined peptides in transfected eukaryotic cells has also previously been established, although not using retroviral vectors (M. S. Malnati et al., Nature, 357, 702-704, 1992., E. O. Long et al., J. Immunol., 153, 1487-1494, 1994). A library of random peptides has never been expressed in mammalian cells with the purpose of identifying biologically active peptides or ribonucleic acids.

DOCUMENT-IDENTIFIER: US 20010051375 A1

TITLE: Highly efficient gene transfer into human repopulating stem cells by RD114 pseudotyped retroviral vector particles

----- KWIC -----

Summary of Invention Paragraph - BSTX (75):

[0068] According to the invention, the gene of interest carried by the RD114 can be any gene pseudotyped vector particle. In a preferred embodiment, the gene of interest is a therapeutically relevant gene. The non-limiting examples of such genes include genes encoding wild-type proteins missing in mutant cells (e.g., factors VII and IX, tumor suppressor genes, etc.) and genes involved in drug resistance or anti-viral resistance (e.g., MDR, ribozymes, antisense RNAs, anti-vital proteases, etc.). Examples of therapeutic genes include polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoA1 and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, e.g., the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; anti-tumor protein intracellular antibodies; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance

(MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent. In one of the embodiments, the invention also discloses the use of a gene of interest encoding a marker gene, such as enhanced green fluorescent protein (EGFP). Such marker genes are particularly useful for tracking the fate of transduced cells, e.g., during clinical development of a gene therapy based on the vectors and methods of the invention.

DOCUMENT-IDENTIFIER: US 20010044654 A1

TITLE: Decellularized vascular prostheses resistant to
thrombus occlusion and immunologic rejection

----- KWIC -----

Summary of Invention Paragraph - BSTX (32):

[0030] It is also an object of the present invention to provide a method of linking decellularized vascular tissue with at least one anti-thrombogenic agent and applying a second linking of at least one cellular growth factor so that the modified vascular tissue may be used as a vascular prosthesis.

DOCUMENT-IDENTIFIER: US 20010044413 A1

TITLE: In situ bioreactors and methods of use thereof

----- KWIC -----

Detail Description Paragraph - DETX (45):

[0072] In certain various embodiments of the invention, the matrix may comprise or be modified, e.g., coated or impregnated, prior to implantation with certain substances to enhance the attachment and growth of cells on the matrix in vivo. These substances include, but are not limited to, bioactive agents such as cellular growth factors (e.g., TGF- β , FGF, etc.), substances that stimulate chondrogenesis (e.g., BMPs that stimulate cartilage formation such as BMP-2, BMP-12 and BMP-13), factors that stimulate migration of cells to the matrix, factors that stimulate matrix deposition, substances or factors that stimulate angiogenesis (e.g., anti-Thrombospondin 2 antibodies), anti-inflammatories (e.g., non-steroidal anti-inflammatories), immunosuppressants (e.g., cyclosporins), as well as other proteins, such as collagens, elastic fibers, reticular fibers, glycoproteins or glycosaminoglycans, such as heparin sulfate, chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate, keratin sulfate, etc. The bioactive agent may also be a cell retention agent, such as laminin, fibronectin or the like to adhere cells to the matrix, or may be an active inhibitor of cellular migration such as macrophage migration inhibitory factor (MIF). One of ordinary skill in the art will readily recognize that such agents may either be in the form of polypeptides or in the form of nucleic acid molecules encoding such polypeptides, such that upon implantation such nucleic acid molecules are taken up by the migrating cells and expressed.

DOCUMENT-IDENTIFIER: US 20010043929 A1

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Summary of Invention Paragraph - BSTX (42):

[0039] A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments, for use in active immunity; cytokines and cellular growth factors, for stimulating immunological inflammatory responses; hormones; and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, Philips, Waldmann).

Summary of Invention Paragraph - BSTX (52):

[0048] (c) a cytokine or cellular growth factor, for use in stimulating an immune response in the subject;

Claims Text - CLTX (4):

3. The method of claim 2, wherein the effector is selected from the group consisting of: (a) an antibody F.sub.ab fragment specific against a pathogen present in the bloodstream, for use in treating the subject for infection by the pathogen; (b) a CD4 glycoprotein, for use in treating the subject for infection by human immunodeficiency virus (HIV); (c) a cytokine or a cellular growth factor, for use in stimulating an immune response in the subject; (d) a polysaccharide which binds to endothelial leukocyte adhesion molecule-(ELAM), for use in treating inflammation related to neutrophil recruitment and tissue infiltration; (e) IL-1 inhibitor or IL-1RA, for treating a subject to achieve immune-response suppression; (f) polymyxin B or polymyxin B decapeptide, for treating the subject for septic shock; and (g) a peptide hormone, for treating a subject to regulate cellular growth.

DOCUMENT-IDENTIFIER: US 20010005720 A1

TITLE: METHOD OF TREATING CHRONIC PROGRESSIVE VASCULAR
SCARRING DISEASES

----- KWIC -----

Detail Description Paragraph - DETX (67):

[0088] The foregoing data, generated by scientifically validated experimental procedures, demonstrate the effectiveness of PPS in decreasing the synthesis of excess extracellular matrix collagen and certain cellular growth factors while increasing the activity of collagen degradation enzymes. These effects indicate that PPS should be highly effective in the clinical management and reversal of CPVSD, particularly arteriosclerosis and atherosclerosis.

US-PAT-NO: 7390895

DOCUMENT-IDENTIFIER: US 7390895 B2

TITLE: Production of polyketides and other natural products

----- KWIC -----

Description Paragraph - DETX (361):

Transplantation. 73(10):1538-42. Foey, A., Green, P., Foxwell, B., Feldmann, M., Brennan, F. (2002). Cytokine-stimulated T cells induce macrophage IL-10 production dependent on phosphatidylinositol 3-kinase and p70S6K: implications for rheumatoid arthritis. *Arthritis Res.* 4(1):64-70. Epub 2001 Oct. 10. Gaisser, S., Reather, J., Wirtz, G., Kellenberger, L., Staunton, J., and Leadlay, P. F. (2000) A defined system for hybrid macrolide biosynthesis in *Saccharopolyspora erythraea*. *Molecular Microbiology* 36: 391-401. Gaisser, S., Lill, R., Staunton, J., Mendez, C., Salas, J., Leadlay, P. F. (2002) Parallel pathways for oxidation of 14-membered polyketide macrolactones in *Saccharopolyspora erythraea*. *Mol Microbiol* 44:771-81. Galat, A. (2000) Sequence diversification of the FK506-binding proteins in several different genomes. *European Journal of Biochemistry* 267: 4945-4959. Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular growth factor and cytokine response in injured vessels. *Transplantation* 55(6):1409-1418. Gregory M A, Till R, Smith, M C M. (in Press) integration site for *Streptomyces* phage .PHI.BT1 and the development of site-specific integrating vectors. *J. Bacteriol.* Guba, M., von Breitenbuch, P., Steinbauer, M., Koehl, G., Flegel, S., Hornung, M., Bruns, C. J., Zuelke, C., Farkas, S., Anthuber, M., Jauch, K. W., and Geissler, E. K. (2002) Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. *Nature Medicine* 8: 128-135. Hamilton, G. S., and Steiner, J. P. (1998) Immunophilins: Beyond immunosuppression. *Journal of Medicinal Chemistry* 41: 5119-5143. Hara, K., Yonezawa, K., Kozlowski, M. T., Sugimoto, T., Andrabi, K., Weng, Q. P., Kasuga, M., Nishimoto, I., and Avruch, J. (1997) Regulation of eIF-4E BP1 phosphorylation by mTOR. *Journal of Biological Chemistry* 272: 26457-26463. Hardwick, J. S., Kuruvilla, F. G., Tong, J. K., Shamji, A. F., and Schreiber, S. L. (1999) Rapamycin-modulated transcription defines the subset of nutrient-sensitive signaling pathways directly controlled by the Tor proteins. *Proceedings of the National Academy of Sciences of the United States of America* 96: 14866-14870. Hatanaka, H., Kino, T., Miyata, S., Inamura, N., Kuroda, A., Goto, T., Tanaka, H., Okuhara, M. (1988). FR-900520 and FR-900523, novel immunosuppressants isolated from a *Streptomyces*. II. Fermentation, isolation and physico-chemical and biological characteristics. *J. Antibiot. (Tokyo)*. 41(11):1592-601. Hatanaka H, Kino T, Asano M, Goto T, Tanaka H, Okuhara M. (1989). FK-506 related compounds produced by *Streptomyces tsukubaensis* No. 9993. *J. Antibiot. (Tokyo)*. 42(4):620-2 Hendrickson, B. A., Zhang, W.,

Craig, R. J., Jin, Y. J., Bierer, B. E., Burakoff, S., and DiLella, A. G. (1993) Structural organization of the genes-encoding human and murine FK506-binding protein (FKBP)13 and comparison to FKBP1. *Gene* 134: 271-275.

Hentges, K. E., Sirry, B., Gingeras, A. C., Sarbassov, D., Sonenberg, N., Sabatini, D., and Peterson, A. S. (2001) FRAP/mTOR is required for proliferation and patterning during embryonic development in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 98: 13796-13801.

Hopwood, D. A. (1997) Genetic contributions to understanding polyketide synthases. *Chemical Reviews* 97: 2465-2497.

Hosted, T. J., and Baltz, R. H. (1997) Use of rpsL for dominance selection and gene replacement in *Streptomyces roseosporus*. *Journal of Bacteriology* 179: 180-186.

Hung, D. T., and Schreiber, S. L. (1992) cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein. *Biochemical and Biophysical Research Communications* 184: 733-738.

Hung, D. T., Jamison, T. F., and Schreiber, S. L. (1996) Understanding and controlling the cell cycle with natural products. *Chemistry & Biology* 3: 623-639.

Jain, S., Bicknell, G. R., Whiting, P. H., Nicholson, M. L. (2001). Rapamycin reduces expression of fibrosis-associated genes in an experimental model of renal ischaemia reperfusion Injury. *Transplant Proc.* 33(1-2):556-8.

Jin, Y. J., Burakoff, S. J., and Bierer, B. E. (1992) Molecular cloning of a 25 kDa high affinity rapamycin binding protein, FKBP25. *Journal of Biological Chemistry* 267: 10942-10945.

Kahan, B. D., Chang, J. Y., and Sehgal, S. N. (1991) Preclinical evaluation of a new potent immunosuppressive agent, rapamycin. *Transplantation* 52: 185-191.

Kahan, B. D., and Camardo, J. S. (2001) Rapamycin: Clinical results and future opportunities. *Transplantation* 72:1181-1193.

Kallen, J. A., Sedrani, R., and Cottens S. (1996) X-ray crystal structure of 28-O-methylrapamycin complexed with FKBP12: Is the cyclohexyl moiety part of the effector domain of rapamycin? *Journal of the American Chemical Society* 118: 5857-5861.

Kawasome, H., Papst, P., Webb, S., Keller, G. M., Johnson, G. L., Gelfand, E. W., and Terada, N. (1998) Targeted disruption of p70.sup.s6k defines its role in protein synthesis and rapamycin sensitivity. *Proceedings of the National Academy of Sciences of the United States of America* 95: 5033-5038.

Khaw, C. E., Bohm, G. A., Metcalfe, S., Staunton, J., and Leadlay, P. F. (1998) Mutational biosynthesis of novel rapamycins by a strain of *Streptomyces hygroscopicus* NRRL 5491 disrupted in rapL, encoding a putative lysine cyclodeaminase. *Journal of Bacteriology* 180: 809-814.

Kieser, T., Bibb, M. J., Buttner, M. J., Chater, K. F., and Hopwood, D. A. (2000) *Practical Streptomyces Genetics*, John Innes Foundation, Norwich.

Kirby, B., and Griffiths, C. E. M. (2001) Psoriasis: the future. *British Journal of Dermatology* 144:3743.

Kirchner, G. I., Winkler, M., Mueller L., Vidal, C., Jacobsen, W., Franzke, A., Wagner, S., Blick, S., Manns M. P., and Sewing K.-F. (2000) Pharmacokinetics of SDZ RAD and cyclosporin including their metabolites in seven kidney graft patients after the first dose of SDZ RAD *British Journal of Clinical Pharmacology* 50:449-454.

Konig, A., Schwecke, T., Molnar, I., Bohm, G., Lowden, P. A. S., Staunton, J., and Leadlay, P. F. (1997) The pipecolate-incorporating enzyme for the biosynthesis of the immunosuppressant rapamycin. Nucleotide sequence analysis, disruption and heterobogus expression of rapP from *Streptomyces hygroscopicus*. *European Journal of Biochemistry* 247: 526-534.

Kunz, J., Loeschmann, A., Deuter-Reinhard, M., and Hall, M. N. (2000) FAP1, a homologue of human

transcription factor NF-X1, competes with rapamycin for binding to FKBP12 in yeast. *Molecular Microbiology* 37: 1480-1493. Kuo, C. J., Chung, J. K., Fiorentino, D. F., Flanagan, W. M., Blenis, J., and Crabtree, G. R. (1992) Rapamycin selectively inhibits interleukin-2 activation of p70 S6 kinase. *Nature* 358: 70-73. Lee, M. H. Pascopella, L., Jacobs, W. R., Jr and Hatfull, G F. (1991). Site specific integration of mycobacteriophage L5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis* and *Bacille Calmette-Guerin*; *Proc. Natl. Acad. Sci. USA*, 88:3111-3115. Lee M H, Pascopella L, Jacobs W R Jr, Hatfull G F. (1991), Site-specific integration of mycobacteriophage L5: integration-proficient vectors for *Mycobacterium smegmatis*, *Mycobacterium tuberculosis*, and *bacille Calmette-Guerin*. *Proc Natl Acad Sci USA*.; 88:3111-5. Liang, J., Choi, J., and Clardy, J. (1999) Refined structure of the FKBP12-rapamycin-FRB ternary complex at 2.2 Å resolution. *Acta Crystallographica Section D-Biological Crystallography* 55: 736-744. Lomovskaya, N., Fonstein, L., Ruan, X., Stassi, D., Katz, L., and Hutchinson, C. R. (1997) Gene disruption and replacement in the rapamycin-producing *Streptomyces hygroscopicus* strain ATCC 29253. *Microbiology-Uk* 143: 875-883. Lowden, P. A. S., Bohm, G., Staunton, J., and Leadlay, P. F. (1996) The nature of the starter unit for the rapamycin polyketide synthase. *Angewandte Chemie* 35: 2249-2251. Lowden, P. A. S., (1997) Ph. D. Dissertation, University of Cambridge. "Studies on the biosynthesis of rapamycin". Lowden, P. A. S., Wilkinson, B., Bohm, G. A., Handa, S., Floss, H. G., Leadlay, P. F., and Staunton, J. (2001) Origin and true nature of the starter unit for the rapamycin polyketide synthase. *Angewandte Chemie-International Edition* 40: 777-779.

US-PAT-NO: 7361330

DOCUMENT-IDENTIFIER: US 7361330 B2

TITLE: Methods of using flt3-ligand in the treatment of
fibrosarcoma

----- KWIC -----

Brief Summary Text - BSTX (40):

The procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Briefly, the term means a method comprising: (1) collecting CD34^{sup.}+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo . In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-ligand, IL-1, IL-3, c-kit ligand, can be used.

US-PAT-NO: 7300942

DOCUMENT-IDENTIFIER: US 7300942 B2

See image for Certificate of Correction

TITLE: Production of polyketides and other natural products

----- KWIC -----

Description Paragraph - DETX (342):

Alarcon, C. M., Heitman, J., and Cardenas, M. E. (1999) Protein kinase activity and identification of a toxic effector domain of the target of rapamycin TOR proteins in yeast. *Molecular Biology of the Cell* 10: 2531-2546. Aparicio, J. F., Molnar, I., Schwecke, T., Konig, A., Haydock, S. F., Khaw, L. E., Staunton, J., and Leadlay, P. F. (1996) Organization of the biosynthetic gene cluster for rapamycin in *Streptomyces hygroscopicus*: analysis of the enzymatic domains in the modular polyketide synthase. *Gene* 169: 916. Baker, H., Sidorowicz, A., Sehgal, S. N., and Vezina, C. (1978) Rapamycin (AY-22,989), a new antifungal antibiotic. III. In vitro and in vivo evaluation. *Journal of Antibiotics* 31: 539-545. Bierman, M., Logan, R., O'Brien, K., Seno, E. T., Nagaraja Rao, R., and Schoner, B. E. (1992) Plasmid cloning vectors for the conjugal transfer of DNA from *Escherichia coli* to *Streptomyces* spp. *Gene* 116: 4349. Blanc, V., Lagneaux, D., Didier, P., Gil, P., Lacroix, P., and Crouzet, J. (1995) Cloning and analysis of structural genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the conversion of pristinamycin II.sub.B to pristinamycin II.sub.A (PII.sub.A): PII.sub.A synthase and NADH:riboflavin 5'-phosphate oxidoreductase. *Journal of Bacteriology* 177: 5206-5214. Blanc, V., Gil, P., Bamas-Jacques, N., Lorenzon, S., Zagorec, M., Schleuniger, J., Bisch, D., Blanche, F., Debussche, L., Crouzet, J., and Thibaut, D. (1997) Identification and analysis of genes from *Streptomyces pristinaespiralis* encoding enzymes involved in the biosynthesis of the 4-dimethylamino-L-phenylalanine precursor of pristinamycin I. *Molecular Microbiology* 23: 191-202. Box, S. J., Shelley, P. R., Tyler, J. W., Verrall, M. S., Warr, S. R. C., Badger, A. M., Levy, M. A., and Banks, R. M. (1995) 27-O-Demethylrapamycin, an immunosuppressant compound produced by a new strain of *Streptomyces hygroscopicus*. *Journal of Antibiotics* 48: 1347-1349. Brown, E. J., Albers, M. W., Shin, T. B., Ichikawa, K., Keith, C. T., Lane, W. S., and Schreiber, S. L. (1994) A mammalian protein targeted by G1-arresting rapamycin-receptor complex. *Nature* 369: 756-758. Brunn, G. J., Williams, J., Sabers, C., Wiederrecht, G., Lawrence, J. C., and Abraham, R. T. (1996) Direct inhibition of the signaling functions of the mammalian target of rapamycin by the phosphoinositide 3-kinase inhibitors, wortmannin and LY294002. *EMBO Journal* 15: 5256-5267. Cao, W., Mohacsi, P., Shorthouse, R., Pratt, R. and Morris, R. E. (1995). Effects of rapamycin on growth factor-stimulated vascular smooth muscle cell DNA synthesis. Inhibition of basic fibroblast growth factor and platelet-derived growth factor action and antagonism of rapamycin by FK506. *Transplantation* 59(3): 390-395. Carlson, R. P., Hartman,

D. A., Tomchek, L. A., Walter, T. L., Lugay, J. R., Calhoun, W., Sehgal, S. N., Chang, J. Y. (1993). Rapamycin, a potential disease-modifying antiarthritic drug. *J. Pharmacol. Exp. Ther.* 266(2):1125-38. Chambraud, B., Radanyi, C., Camonis, J. H., Shazand, K., Rajkowski, K, and Baulieu, E. E. (1996) FAP48, a new protein that forms specific complexes both immunophilins FKBP59 and FKBP12. Prevention by the immunosuppressant drugs FK506 and rapamycin. *Journal of Biological Chemistry* 271: 32923-32929. Chang, J. Y., Sehgal, S. N., and Bansbach, C. C. (1991) FK506 and rapamycin: novel pharmacological probes of the immune response. *Trends in Pharmacological Sciences* 12: 218-223. Chen, J., Zheng, X. F., Brown, E. J., and Schreiber, S. L. (1995) Identification of an 11-kDa FKBP12-rapamycin-binding domain within the 289-kDa FKBP12-rapamycin-associated protein and characterization of a critical serine residue. *Proceedings of the National Academy of Sciences of the United States of America* 92: 4947-4951. Chini, M., Crotti, P., Gardelli, C., and Macchia, F., (1992), *Tetrahedron*, 48, 3805-3812 Choi, J. W., Chen, J., Schreiber, S. L., and Clardy, J. (1996) Structure of the FKBP12-rapamycin complex interacting with the binding domain of human FRAP. *Science* 273: 239-242. Chung, L., Liu, L., Patel, S., Carney, J. R., and Reeves, C. D. (2001) Deletion of rapQNML from the rapamycin gene cluster of *Streptomyces hygroscopicus* gives production of the 16-O-desmethyl-27-desmethoxy analog. *Journal of Antibiotics* 54: 250-256. Corey, E. J. and Huang, H., (1989) *Tetrahedron Lett.*, 30, 5235-5238 DiLella, A. G., and Craig, R. J. (1991) Exon organization of the human FKBP-12 gene: correlation with structural and functional protein domains. *Biochemistry* 30: 8512-8517. Du, L. C., Sanchez, C., Chen, M., Edwards, D. J., and Shen, B. (2000) The biosynthetic gene cluster for the antitumor drug bleomycin from *Streptomyces verticillus* ATCC15003 supporting functional interactions between nonribosomal peptide synthetases and a polyketide synthase. *Chemistry & Biology* 7: 623-642. Dudkin, L., Dilling, M. B., Cheshire, P. J., Hanwood, F. C., Hollingshead, M., Arbuck, S. G., Travis, R., Sausville, E. A., Houghton, P. J. (2001). Biochemical correlates of mTOR inhibition by the rapamycin ester CCI-779 and tumor growth inhibition. *Clin. Cancer Res.* 7(6):1758-64 Fehr, T., Sanglier, J-J., Schuler, W., Gschwind, L., Ponelle, M., Schilling, W., Wioland, C. (1996). Antascomicin A, B, C, D and E: Novel FKBP12 binding compounds from a *Micromonospora* strain. *J. Antibiot.* 49(3): 230-233. Ferrari, S., Pearson, R. B., Siegmann, M., Kozma, S. C., and Thomas, G. (1993) The immunosuppressant rapamycin induces inactivation of p70.s6k through dephosphorylation of a novel set of sites. *Journal of Biological Chemistry* 268: 16091-16094. Findlay J. A, and Radics, L. (1980) *Canadian Journal of Chemistry* 58:579. Fishbein, T. M., Florman, S., Gondolesi, G., Schiano, T., LeLeiko, N., Tschemia, A., Kaufman, S. (2002). Intestinal transplantation before and after the introduction of sirolimus. *Transplantation.* 73(10): 1538-42. Foey, A., Green, P., Foxwell, B., Feldmann, M., Brennan, F. (2002). Cytokine-stimulated T cells induce macrophage IL-10 production dependent on phosphatidylinositol 3-kinase and p70S6K: implications for rheumatoid arthritis. *Arthritis Res.* 4(1):64-70. Epub 2001 Oct. 10. Gaisser, S., Reather, J., Wirtz, G., Kellenberger, L., Staunton, J., and Leadlay, P. F. (2000) A defined system for hybrid macrolide biosynthesis in *Saccharopolyspora erythraea*. *Molecular Microbiology* 36: 391-401. Gaisser, S., Lill, R., Staunton, J., Mendez, C., Salas, J., Leadlay, P F. (2002) Parallel pathways for oxidation of 14-membered

polyketide macrolactones in *Saccharopolyspora erythraea*. *Mol Microbiol* 44:771-81. Galat, A. (2000) Sequence diversification of the FK506-binding proteins in several different genomes. *European Journal of Biochemistry* 267: 4945-4959. Gregory, C. R., Huie, P., Billingham, M. E. and Morris, R. E. (1993). Rapamycin inhibits arterial intimal thickening caused by both alloimmune and mechanical injury. Its effect on cellular growth factor and cytokine response in injured vessels. *Transplantation* 55(6):1409-1418.

Gregory M A, Till R, Smith, M C M. (in Press) Integration site for *Streptomyces* phage ϕ .BT1 and the development of site-specific integrating vectors. *J Bacteriol.*

Guba, M., von Breitenbuch, P., Steinbauer, M., Koehl, G., Flegel, S., Hornung, M., Bruns, C. J., Zuelke, C., Farkas, S., Anthuber, M., Jauch, K. W., and Geissler, E. K (2002) Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. *Nature Medicine* 8: 128-135.

Hamilton, G. S., and Steiner, J. P. (1998) Immunophilins: Beyond immunosuppression. *Journal of Medicinal Chemistry* 41: 5119-5143.

Hara, K., Yonezawa, K., Kozlowski, M. T., Sugimoto, T., Andrabi, K., Weng, Q. P., Kasuga, M., Nishimoto, I., and Avruch, J. (1997) Regulation of eIF-4E BP1 phosphorylation by mTOR. *Journal of Biological Chemistry* 272: 26457-26463.

Hardwick, J. S., Kuruvilla, F. G., Tong, J. K, Shamji, A. F., and Schreiber, S. L. (1999) Rapamycin-modulated transcription defines the subset of nutrient-sensitive signaling pathways directly controlled by the Tor proteins. *Proceedings of the National Academy of Sciences of the United States of America* 96: 14866-14870.

Hatanaka, H., Kino, T., Miyata, S., Inamura, N., Kuroda, A, Goto, T., Tanaka, H., Okuhara, M. (1988). FR-900520 and FR-900523, novel immunosuppressants isolated from a *Streptomyces*. II. Fermentation, isolation and physico-chemical and biological characteristics. *J. Antibiot. (Tokyo)*. 41(11):1592-601.

Hatanaka H, Kino T, Asano M, Goto T, Tanaka H, Okuhara M. (1989). FK-506 related compounds produced by *Streptomyces tsukubaensis* No. 9993. *J. Antibiot. (Tokyo)*. 42(4):620-2.

Hendrickson, B. A., Zhang, W., Craig, R. J., Jin, Y. J., Bierer, B. E., Burakoff, S., and DiLella, A. G. (1993) Structural organization of the genes encoding human and murine FK506-binding protein (FKBP)13 and comparison to FKBP1. *Gene* 134: 271-275.

Hentges, K. E., Sirry, B., Gingeras, A. C., Sarbassov, D., Sonenberg, N., Sabatini, D., and Peterson, A. S. (2001) FRAP/mTOR is required for proliferation and patterning during embryonic development in the mouse. *Proceedings of the National Academy of Sciences of the United States of America* 98: 13796-13801.

Hopwood, D. A. (1997) Genetic contributions to understanding polyketide synthases. *Chemical Reviews* 97: 2465-2497.

Hosted, T. J., and Baltz, R. H. (1997) Use of rpsL for dominance selection and gene replacement in *Streptomyces roseosporus*. *Journal of Bacteriology* 179: 180-186.

Hung, D. T., and Schreiber, S. L. (1992) cDNA cloning of a human 25 kDa FK506 and rapamycin binding protein. *Biochemical and Biophysical Research Communications* 184: 733-738.

Hung, D. T., Jamison, T. F., and Schreiber, S. L. (1996) Understanding and controlling the cell cycle with natural products. *Chemistry & Biology* 3: 623-639.

Jain, S., Bicknell, G. R., Whiting, P. H., Nicholson, M. L. (2001). Rapamycin reduces expression of fibrosis-associated genes in an experimental model of renal ischaemia reperfusion injury. *Transplant Proc.* 33(1-2):556-8.

Jin, Y. J., Burakoff, S. J., and Bierer, B. E. (1992) Molecular cloning of a 25-kDa high affinity rapamycin binding protein, FKBP25. *Journal*

of Biological Chemistry 267: 10942-10945. Kahan, B. D., Chang, J. Y., and Sehgal, S. N. (1991) Preclinical evaluation of a new potent immunosuppressive agent, rapamycin. Transplantation 52: 185-191. Kahan, B. D., and Camardo, J. S. (2001) Rapamycin: Clinical results and future opportunities. Transplantation 72:1181-1193. Kallen, J. A., Sedrani, R., and Cottens S. (1996) X-ray crystal structure of 28-O-methylrapamycin complexed with FKBP12: Is the cyclohexyl moiety part of the effector domain of rapamycin? Journal of the American Chemical Society 118: 5857-5861. Kawasome, H., Papst, P., Webb, S., Keller, G. M., Johnson, G. L., Gelfand, E. W., and Terada, N. (1998) Targeted disruption of p70.sup.s6k defines its role in protein synthesis and rapamycin sensitivity. Proceedings of the National Academy of Sciences of the United States of America 95: 5033-5038. Khaw, L. E., Bohm, G. A., Metcalfe, S., Staunton, J., and Leadlay, P. F. (1998) Mutational biosynthesis of novel rapamycins by a strain of Streptomyces hygroscopicus NRRL 5491 disrupted in rapL, encoding a putative lysine cyclodeaminase. Journal of Bacteriology 180: 809-814. Kieser, T., Bibb, M. J., Buttner, M. J., Chater, K. F., and Hopwood, D. A. (2000) Practical Streptomyces Genetics, John Innes Foundation, Norwich. Kirby, B., and Griffiths, C. E. M. (2001) Psoriasis: the future. British Journal of Dermatology 144:37-43. Kirchner, G. I., Winkler, M., Mueller L., Vidal, C., Jacobsen, W., Franzke, A., Wagner, S., Blick, S., Manns M. P., and Sewing K.-F.(2000) Pharmacokinetics of SDZ RAD and cyclosporin including their metabolites in seven kidney graft patients after the first dose of SDZ RAD. British Journal of Clinical Pharmacology 50:449-454. Konig, A., Schwecke, T., Molnar, I., Bohm, G., Lowden, P. A. S., Staunton, J., and Leadlay, P. F. (1997) The pipecolate-incorporating enzyme for the biosynthesis of the immunosuppressant rapamycin. Nucleotide sequence analysis, disruption and heterologous expression of rapP from Streptomyces hygroscopicus. European Journal of Biochemistry 247: 526-534. Kunz, J., Loeschmann, A., Deuter-Reinhard, M., and Hall, M. N. (2000) FAP1, a homologue of human transcription factor NF-X1, competes with rapamycin for binding to FKBP12 in yeast. Molecular Microbiology 37: 1480-1493. Kuo, C. J., Chung, J. K., Fiorentino, D. F., Flanagan, W. M., Blenis, J., and Crabtree, G. R. (1992) Rapamycin selectively inhibits interleukin-2 activation of p70 S6 kinase. Nature 358: 70-73. Lee, M. H. Pascopella, L., Jacobs, W. R., Jr and Hatfull, G. F (1991). Site specific integration of mycobacteriophage L5: integration-proficient vectors for Mycobacterium smegmatis, Mycobacterium tuberculosis and Bacille Calmette-Guerin. Proc. Natl. Acad. Sci. USA, 88:3111-3115. Lee M H, Pascopella L, Jacobs W R Jr, Hatfull G F. (1991), Site-specific integration of mycobacteriophage L5: integration-proficient vectors for Mycobacterium smegmatis, Mycobacterium tuberculosis, and bacille Calmette-Guerin. Proc Natl Acad Sci USA.; 88:3111-5. Liang, J., Choi, J., and Clardy, J. (1999) Refined structure of the FKBP12-rapamycin-FRB ternary complex at 2.2 .ANG. resolution. Acta Crystallographica Section D-Biological Crystallography 55: 736-744. Lomovskaya, N., Fonstein, L., Ruan, X., Stassi, D., Katz, L., and Hutchinson, C. R. (1997) Gene-disruption and replacement-in the rapamycin-producing Streptomyces hygroscopicus strain ATCC 29253. Microbiology-Uk 143: 875-883. Lowden, P. A. S., Bohm, G., Staunton, J., and Leadlay, P. F. (1996) The nature of the starter unit for the rapamycin polyketide synthase. Angewandte Chemie 35: 2249-2251. Lowden, P. A. S., (1997)

Ph.D. Dissertation, University of Cambridge. "Studies on the biosynthesis of rapamycin". Lowden, P. A. S, Wilkinson, B., Bohm, G. A., Handa, S., Floss, H. G., Leadlay, P. F., and Staunton, J. (2001) Origin and true nature of the starter unit for the rapamycin polyketide synthase. *Angewandte Chemie-International Edition* 40: 777-779. Luengo, J. I., Yamashita, D. S., Dunnington, D., Beck, A. K., Rozamus, L. W., Yen, H. K, Bossard, M. J., Levy, M. A., Hand, A., Newmantarr, T., Badger, A., Faucette, L, Johnson, R. K., Dalessio, K, Porter, T., Shu, A. Y. L, Heys, R., Choi, J. W., Kongsaree, P., Clardy, J., and Holt, D. A. (1995) Structure-Activity Studies of Rapamycin Analogs--Evidence That the C-7 Methoxy Group Is Part of the Effector Domain and Positioned at the Fkbp12-Frap Interface. *Chemistry & Biology* 2: 471-481. Lyons, W. E., George, E. B., Dawson, T. M., Steiner, J. P., and Snyder, S. H. (1994) Immunosuppressant FK506 promotes neurite outgrowth in cultures of PC12 cells and sensory ganglia. *Proceedings of the National Academy of Sciences of the United States of America* 91:3191-3195. MacNeil, D. J., Gewain, K. M., Ruby, C. L., Dezeny, G., Gibbons, P. H., and MacNeil, T. (1992) Analysis of *Streptomyces avermitilis* genes required for avermectin biosynthesis utilizing a novel integration vector. *Gene* 111: 61-68. Marahiel, M. A., Stachelhaus, T., and Mootz, H. D. (1997) Modular peptide synthetases involved in nonribosomal peptide synthesis. *Chemical Reviews* 97: 2651-2673. Matsuura, M., Noguchi, T., Yamaguchi, D., Aida, T., Asayama, M., Takahashi, H. and Shirai, M. (1996). The sre gene (ORF469) encodes a site-specific recombinase responsible for integration of the R4 phage genome. *J Bact.* 178(11):3374-3376. McAlpine, J. B., Swanson S. J., Jackson, M., Whittern, D. N. (1991). Revised NMR assignments for rapamycin. *Journal of Antibiotics* 44: 688-690. Meo, T. in "Immunological Methods", L. Lefkovits and B. Pernis, Eds., Academic Press, N.Y. pp. 227-239 (1979). Molnar, I., Aparicio, J. F., Haydock, S. F., Khaw, L. E., Schwecke, T., Konig, A., Staunton, J., and Leadlay, P. F. (1996) Organisation of the biosynthetic gene cluster for rapamycin in *Streptomyces hygroscopicus*: analysis of genes flanking the polyketide synthase. *Gene* 169: 1-7. Morice, M. C., Serruys, P. W., Sousa, J. E., Fajadet, J., Ban Hayashi, E., Perin, M., Colombo, A., Schuler, G., Barragan, P., Guagliumi, G., Molnar, F., Falotico, R. (2002). RAVEL Study Group. Randomized Study with the Sirolimus-Coated Bx Velocity Balloon-Expandable Stent in the Treatment of Patients with de Novo Native Coronary Artery Lesions. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N. Engl. J. Med.* 346(23):1773-80. Motamedi, H., Shafiee, A., Cai, S. J., Streicher, S. L., Arison, B. H., and Miller, R. R. (1996) Characterization of methyltransferase and hydroxylase genes involved in the biosynthesis of the immunosuppressants FK506 and FK520. *Journal of Bacteriology* 178: 5243-5248. Motamedi, H., Cai, S. J., Shafiee, A., and Elliston, K. O. (1997) Structural organization of a multifunctional polyketide synthase involved in the biosynthesis of the macrolide immunosuppressant FK506. *European Journal of Biochemistry* 244: 74-80. Motamedi, H., and Shafiee, A. (1998) The biosynthetic gene cluster for the macrolactone ring of the immunosuppressant FK506. *European Journal of Biochemistry* 256: 528-534. Myckatyn, T. M., Ellis, R. A., Grand, A. G., Sen, S. K., Lowe, J. B. 3rd, Hunter, D. A., Mackinnon, S. E. (2002). The effects of rapamycin in murine peripheral nerve isografts and allografts. *Plast. Reconstr. Surg.*

US-PAT-NO: 7244707

DOCUMENT-IDENTIFIER: US 7244707 B2

TITLE: Regulation of cytotrophoblast cell differentiation and
cell migration

----- KWIC -----

Abstract Text - ABTX (1):

The present invention is predicated on the discovery of certain interactions between cellular growth factors and opposing actions that control differentiation and migration or invasion of cytotrophoblasts into the uterine endometrium during pregnancy. IGF-II and latent transforming growth factor beta (TGF.beta.), the inactive precursor of TGF.beta., compete for binding to the CIM6P receptor. IGF-II prevents latent TGF.beta. binding to the CIM6P receptor. The invention therefore offers a method of regulating and directing cytotrophoblast differentiation and function based on the interaction between IGF-II, latent TGF.beta. and the CIM6P receptor. There is disclosed a method of regulating cytotrophoblast and stem cell differentiation and migration characterized by adjusting levels of insulin-like growth factor II (IGF-II) available for binding to the cation-independent mannose-6-phosphate (CIM6P) receptor. The discovery may be applied to embryonic or adult stem cells to control their differentiation and migratory behaviour.

Brief Summary Text - BSTX (16):

The present invention is predicated on the discovery of certain interactions between cellular growth factors and opposing actions that control differentiation and migration or invasion of cytotrophoblasts into the uterine endometrium which, during pregnancy, is called the decidua. In addition, this discovery may be applied to embryonic or adult stem cells to control their differentiation and migratory behaviour.

US-PAT-NO: 7232566

DOCUMENT-IDENTIFIER: US 7232566 B2

TITLE: Methods for treating HIV infected subjects

----- KWIC -----

Description Paragraph - DETX (170):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 7220538

DOCUMENT-IDENTIFIER: US 7220538 B2

TITLE: Composition for maintaining organ and cell viability

----- KWIC -----

Brief Summary Text - BSTX (12):

In one aspect of the invention there is provided a two-phase composition for maintaining cellular viability. The composition includes a first phase comprising a base nutritive medium; and a second phase comprising nanoparticles having an outer lipophilic coating and an inner hydrophilic core, wherein a) the first phase comprises physiologically compatible concentrations/ amounts of water soluble or dispersible nutrients, and physiological salts; b) the nanoparticles of the second phase comprise one or more of the following: lipids, fatty acids, sterols, free fatty acids, optional cellular growth factors; and c) the two-phase composition has an osmolality of at least about 300 mOsM/kg.

Description Paragraph - DETX (28):

In another preferred embodiment, the second phase also includes hydrophilic supportive endocrine factors such as hydrocortisone, thyroxine or its derivatives, and the like. Further supportive components can include, for example, cellular growth factors, e.g., epithelial and endothelial growth factors, including physiologically compatible amounts of vascular endothelial growth factor, platelet derived endothelial growth factor, epithelial growth factor, hepatocyte growth factor, platelet derived endothelial growth factor, and the like. Optionally, other factors contemplated to be included in the second phase include intercellular messengers such as prostoglandins, e.g., prostaglandin E1. Preferably, physiologically compatible surfactants and detergents are also included, e.g., one or more water-soluble surfactants, preferably an amphiphilic block copolymer with a molecular weight of several thousand Daltons, such as a polypropyleneoxide-polyethyleneoxide block copolymer surfactant (e.g., Pluronic F-68; from BASF) and/or nonionic surfactants. Suitable nonionic surfactants include, e.g., polyoxyethylene derivatives of sorbitol esters, e.g., polyoxyethylene sorbitan monooleate surfactants that are commercially available as TWEEN.RTM. (Atlas Chemical Co.). TWEEN 80.RTM. is particularly preferred. The core portion of the two-phase compositions of the invention preferably do not include a pharmaceutically significant quantity of a phosphatidic acid or sugar, or a lysophosphatidic acid or sugar.

Claims Text - CLTX (7):

6. The two-phase composition of claim 1, further comprising cellular growth factors.

Claims Text - CLTX (8):

7. The two-phase composition of claim 6, wherein said cellular growth factors are selected from the group consisting of epithelial and endothelial growth factors, vascular endothelial growth factors, platelet derived endothelial growth factors, epithelial growth factors, hepatocyte growth factors, and mixtures thereof.

US-PAT-NO: 7202226

DOCUMENT-IDENTIFIER: US 7202226 B2

TITLE: Augmentation of wound healing by eIF-4E mRNA and EGF mRNA

----- KWIC -----

Description Paragraph - DETX (9):

Specifically, the present invention also provides a method to augment wound healing by intracellular delivery of mRNA encoding translation initiation factor eIF4E in combination with mRNA encoding cellular growth factors such as EGF. Biolistic treatment of incisional wounds with eIF4E mRNA and EGF mRNA augments wound healing in normal animals to a greater extent than animals treated with eIF4E mRNA or EGF alone. This synergistic effect was not predicted. In fact, based upon the prior art, it was unexpected that mRNA would have a predictable effect in vivo.

US-PAT-NO: 7202207

DOCUMENT-IDENTIFIER: US 7202207 B2

See image for Certificate of Correction

TITLE: Indications of mannan-binding lectin (MBL) in the
treatment of immunocompromised individuals

----- KWIC -----

Description Paragraph - DETX (28):

Other biologic and immunomodulating agents have been used in treatment of patients with neutropenia and fever. Intravenous immunoglobulin has no benefit in preventing fever or infection in patients with neutropenia but may have a moderate effect in patients with antibody deficiencies. Interferon gamma may add a benefit to patients with some neutrophil deficiencies, but this is not finally proven. Cellular growth factors (granulocyte and granulocyte-macrophage colony-stimulating factor) may shorten the duration of neutropenia and thus the need for antibiotics.

US-PAT-NO: 7202079

DOCUMENT-IDENTIFIER: US 7202079 B2

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Description Paragraph - DETX (69):

Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, AppAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

US-PAT-NO: 7198793

DOCUMENT-IDENTIFIER: US 7198793 B2

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Description Paragraph - DETX (69):

Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

US-PAT-NO: 7195888

DOCUMENT-IDENTIFIER: US 7195888 B2

TITLE: Calcium-independent phospholipase A2 induces ischemic ventricular arrhythmias and decreases infarction size

----- KWIC -----

Description Paragraph - DETX (78):

The function of complex biological organisms relies on the meticulous control of cellular activity, including close regulation of cell growth, proliferation and function. The family of enzymes known as the phospholipases A.sub.2 has been implicated in the control of cellular activity by catalyzing the esterolytic cleavage of fatty acids from phospholipids, thereby regulating the release of lipid second messengers, cellular growth factors, and the properties of the cellular membrane (Samuelsson et al., Annu. Rev. Biochem. 47:997 1029, 1978; Moolenaar, W. H., Curr. Opin. Cell. Biol. 7:203 10, 1995). In particular, by controlling the production of second messengers such as arachidonic acid and its biologically active eicosanoid metabolites, the phospholipases A.sub.2 are involved in modulating such processes as cellular growth programs, inflammation, vascular tone and ion channel function. (Needleman et al., Annu. Rev. Biochem. 55:69 102, 1986).

US-PAT-NO: 7183381

DOCUMENT-IDENTIFIER: US 7183381 B2

TITLE: Composition of lactoferrin related peptides and uses thereof

----- KWIC -----

Description Paragraph - DETX (211):

A wound is also further defined as a chronic wound. Examples of chronic wounds or chronic ulcers include, but are not limited to diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Yet further, chronic wounds can also include infected wounds. Chronic wounds are wounds that do not repair or do so extremely slowly, and show partial or total lack of structural organization and functional coordination with normal tissue. Chronic wounds or chronic ulcers can be broadly classified into three major types: diabetic ulcers, venous stasis ulcers, decubitus or pressure ulcers. Diabetic ulcers often occur on a foot. Chronic diabetic state and poor glucose control results in poor peripheral circulation and microcirculation due to progressive arteriosclerosis; neuropathic changes that result in an insensate extremity prone to trauma; and intrinsic defects in the wound healing process that may include reduced abundance and response to cellular growth factors. In the case of venous ulcers, venous hypertension causes disturbed microcirculation and pathological changes of the capillaries, elevated persistent levels of pro-inflammatory cytokines and proteases. Fibroblast senesce and respond less to growth factors, which distribute unfavorably. Proteolytic enzymes and their inhibitors are imbalanced. Pressure ulcers occur when skin is under pressure without movement to allow blood flow for 8 12 hours.

US-PAT-NO: 7175843

DOCUMENT-IDENTIFIER: US 7175843 B2

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Description Paragraph - DETX (95):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0×10^6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5×10^6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0×10^6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 7173006

DOCUMENT-IDENTIFIER: US 7173006 B2

TITLE: Drug comprising synthetic peptide analogs for the
treatment of cancer

----- KWIC -----

Brief Summary Text - BSTX (11):

The receptor tyrosine kinases (RTK) are transactivated by G protein coupled receptors (GPCR). Platelet derived growth factor (PDGF), epidermal growth factor (EGF) and insulin like growth factor 1 (IGF1) are tyrosine phosphorylated subsequent to GPCR activation. The phosphorylated growth factors in turn recruit multiple accessory proteins to activate the mitogen activated protein kinases (MAPK). Human adenocarcinomas have increased constitutive MAPK activity (Ostrowski et al, Br. J Cancer Vol 78, 1301 1306, 1997), and the blockade of this protein kinase suppresses tumour growth in vitro and in vivo (Sebolt-Leopold et al, Nature Medicine, Vol 5, 810 816, 1999). The MAP Kinase pathway is a crucial convergence point for many cytoplasmic signaling networks. MAP kinases form a family of Ser/Thr kinases, which can be activated by cellular growth factors. MAP Kinase lies downstream of the Ras-Raf oncogenic pathway and its activation leads to phosphorylation of nuclear transcription factors resulting in cell proliferation (Ostrowski et al., Br. J Cancer Vol 78, 1301 1306, 1997).

US-PAT-NO: 7160554

DOCUMENT-IDENTIFIER: US 7160554 B2

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (42):

A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments, for use in active immunity; cytokines and cellular growth factors, for stimulating immunological inflammatory responses; hormones; and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, Philips, Waldmann).

Brief Summary Text - BSTX (52):

(c) a cytokine or cellular growth factor, for use in stimulating an immune response in the subject;

Claims Text - CLTX (2):

2. The composition of claim 1 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (8):

8. The composition of claim 7 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (14):

14. The composition of claim 13 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (20):

20. The composition of claim 19 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1

inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (26):

26. The composition of claim 25 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (32):

32. The composition of claim 31 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (38):

38. The composition of claim 37 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (44):

44. The composition of claim 43 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

US-PAT-NO: 7153512

DOCUMENT-IDENTIFIER: US 7153512 B2

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Description Paragraph - DETX (69):

Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

US-PAT-NO: 7150992

DOCUMENT-IDENTIFIER: US 7150992 B1

TITLE: Methods of preparing dendritic cells with flt3-ligand and antigen

----- KWIC -----

Description Paragraph - DETX (12):

The procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Briefly, the term means a method comprising: (1) collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-ligand, IL-1, IL-3, c-kit ligand, can be used.

US-PAT-NO: 7150882

DOCUMENT-IDENTIFIER: US 7150882 B2

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (4):

A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments for use in active immunity, cytokines and cellular growth factors for stimulating immunological inflammatory responses, hormones, and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, N. V., et al., Proc. Natl. Acad. Sci. USA 84:1487 1491 (1987); Philips, M. L., et al., Science 250:1130 1132 (1990); Waldmann, T. A., Annu. Rev. Immunol. 10:675 704 (1992)).

Brief Summary Text - BSTX (14):

(c) a cytokine or a cellular growth factor, for use in stimulating an immune response in the subject;

Claims Text - CLTX (2):

2. The composition of claim 1, wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (8):

8. The composition of claim 7 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (14):

14. The composition of claim 13 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (20):

20. The composition of claim 19 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors,

ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (26):

26. The composition of claim 25 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (32):

32. The composition of claim 31 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (38):

38. The composition of claim 37 wherein the effector molecule is selected from the group consisting of Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (44):

44. The composition of claim 43 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

US-PAT-NO: 7144575

DOCUMENT-IDENTIFIER: US 7144575 B2

See image for Certificate of Correction

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Description Paragraph - DETX (157):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6/ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6/ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6/ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 7138275

DOCUMENT-IDENTIFIER: US 7138275 B2

TITLE: Dedifferentiated, programmable stem cells of monocytic origin, and their production and use

----- KWIC -----

Brief Summary Text - BSTX (11):

The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) isolating the monocytes from human blood; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (12):

The present invention includes and provides a process for the production of dedifferentiated, programmable stem cells of human monocytic origin, comprising (a) providing human monocytes; (b) propagating the monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating the monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

Brief Summary Text - BSTX (17):

The present invention includes and provides a dedifferentiated, programmable stem cell of human monocytic origin manufactured by a process comprising (a) isolating monocytes from human blood; (b) propagating monocytes in a culture medium, which contains cellular growth factor M-CSF; (c) simultaneously cultivating monocytes with or subsequently to step (b) in a culture medium comprising IL-3; and (d) obtaining human adult dedifferentiated programmable stem cells by separating from culture medium.

US-PAT-NO: 7125712

DOCUMENT-IDENTIFIER: US 7125712 B2

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Description Paragraph - DETX (69):

Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

US-PAT-NO: 7109029

DOCUMENT-IDENTIFIER: US 7109029 B2

TITLE: Vector constructs

----- KWIC -----

Description Paragraph - DETX (50):

DNA sequences encoding therapeutic genes which may be placed into the vector construct include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-gamma; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. The DNA sequence encoding the therapeutic gene may preferredly be selected from either GM-CSF, thymidine kinase, Nos, FasL, or sFasR (soluble Fas receptor).

US-PAT-NO: 7070592

DOCUMENT-IDENTIFIER: US 7070592 B2

TITLE: Medical device with array of electrode-containing
reservoirs

----- KWIC -----

Description Paragraph - DETX (38):

A wide variety of molecules can be contained in and released from the microchip devices. Examples of the molecules include drugs, diagnostic reagents, fragrances, dyes or coloring agents, sweeteners and other flavoring agents, and compounds used in tissue culture, such as cellular growth factors.

US-PAT-NO: 7067245

DOCUMENT-IDENTIFIER: US 7067245 B2

TITLE: Selection methods

----- KWIC -----

Description Paragraph - DETX (112):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Description Paragraph - DETX (116):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 7067118

DOCUMENT-IDENTIFIER: US 7067118 B2

TITLE: Methods of using mutant flt3-ligand polypeptides to
induce cellular expansion

----- KWIC -----

Description Paragraph - DETX (57):

A procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in detail in U.S. Pat. No. 5,199,942. Briefly, the method includes the steps of collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants and expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3, or c-kit ligand can be used.

US-PAT-NO: 7060022

DOCUMENT-IDENTIFIER: US 7060022 B2

TITLE: Decellularized vascular prostheses resistant to thrombus
occlusion and immunological rejection

----- KWIC -----

Brief Summary Text - BSTX (32):

It is also an object of the present invention to provide a method of linking decellularized vascular tissue with at least one anti-thrombogenic agent and applying a second linking of at least one cellular growth factor so that the modified vascular tissue may be used as a vascular prosthesis.

US-PAT-NO: 7022711

DOCUMENT-IDENTIFIER: US 7022711 B2

TITLE:

2-(4-Pyridyl)amino-6-dialkoxyphenyl-pyrido[2,3-d]pyrimidin-7-ones

----- KWIC -----

Brief Summary Text - BSTX (4):

Angiogenesis is the formation of capillaries from preexisting vessels, generally occurring in the embryo and adult mammalian organisms as part of normal growth and repair, such as wound healing. However, uncontrolled angiogenesis is also associated with cellular proliferative disorders such as cancer, diabetic retinopathy, macular degeneration, psoriasis, rheumatoid arthritis, atheroma, Kaposi's sarcoma, and haemangioma. Solid tumor growth and invasion depend upon an adequate blood supply to provide cellular growth factors, nutrients, and to remove metabolic by-products from active cell division.

US-PAT-NO: 7011973

DOCUMENT-IDENTIFIER: US 7011973 B1

TITLE: Regulatory sequences capable of conferring expression of
a heterologous DNA sequence in endothelial cells in vivo
and uses thereof

----- KWIC -----

Brief Summary Text - BSTX (32):

The endothelial cell-specific regulatory sequences of the invention may also be used in gene therapy to promote angiogenesis to treat diseases such as peripheral vascular disease or coronary artery disease (Isner, Circulation 91 (1995), 2687-2692). For example, the regulatory sequences of the invention can be operatively linked to sequences encoding cellular growth factors which promote angiogenesis, e.g., VEGF, acidic fibroblast growth factor, basic fibroblast growth factor and the like.

US-PAT-NO: 7005513

DOCUMENT-IDENTIFIER: US 7005513 B1

TITLE: Functionalized glycosaminoglycan polymer and medical instruments and drugs by using the same

----- KWIC -----

Abstract Text - ABTX (1):

The present invention provides a functionalized polymer which can be used extensively in the field of medical drugs as well as medical devices and which is obtainable in an organic synthetic manner from glycosaminoglycan controlling adhesion, migration and proliferation of cells via linkage to various cellular growth factors or cytokines or direct interactions with the cells. The functionalized polymer of the present invention is characterized in that it comprises a carbohydrate corresponding to at least a part of the basic structure of glycosaminoglycan introduced into a vinyl-type polymer chain.

US-PAT-NO: 7001925

DOCUMENT-IDENTIFIER: US 7001925 B1

TITLE: Compounds and method for enhancing the efficacy of
anti-cancer drugs

----- KWIC -----

Brief Summary Text - BSTX (5):

Polyamines are naturally occurring amines, which form polycations in vivo. These stabilize DNA architectures and are cellular growth factors. All cells contain some form of the native polyamines: putrescine, spermidine or spermine. Rapidly dividing cells (such as cancer cells) require large amounts of polyamines, and cells can either biosynthesize or import these essential growth factors. Many tumor cell lines have been shown to have very high levels of polyamines and an active polyamine transporter.

US-PAT-NO: 6998234

DOCUMENT-IDENTIFIER: US 6998234 B2

TITLE: Methods for cancer prognosis and diagnosis relating to
tumor vascular endothelial cells

----- KWIC -----

Brief Summary Text - BSTX (11):

Although mechanisms of angiogenesis in normal tissues have been extensively studied using traditional molecular biology, biochemical and immunological methods (reviewed in Saaristo et al., 2000, *Oncogene* 19: 6122-6129), the prior art contains sparse disclosure relating to differential gene expression in VECs. Li et al. (2001, *J. Cereb. Blood Flow Metab.* 21: 61-68) developed a protocol for purifying mRNA from isolated normal rat brain capillaries and subsequent microarray analysis of genes selectively expressed in the blood-brain barrier. They identified a series of over 40 novel gene sequences and known genes, including tissue plasminogen activator (TPA), insulin-like growth factor-2, regulators of G protein signaling, etc.), that had not been known to be specific for the blood-brain barrier functions. Similar experiments on normal bone marrow VEC using Atlas cDNA gene arrays showed the presence of mRNAs of several hematopoietic stimulators, cytokines and interleukins, in these cells (Li et al., 2000, *Cytokine* 12: 1017-1023). cDNA microarray analysis of 268 human VEC genes following infection with *Chlamydia pneumoniae* compared with uninfected endothelial cells revealed 20 genes up-regulated in response to *C. pneumoniae* infection, including cytokines (IL-1), chemokines (IL-8, monocyte chemotactic protein 1), and cellular growth factors, including basic fibroblast growth factor (bFGF) and epidermal growth factor (EGF) (Coombes et al., 2001, *Infect. Immunol.* 69: 1420-1427). Microarray-based evaluation of transcriptional profiles of mechanically induced genes in normal human aortic VEC using vascular endothelial growth factor (VEGF) as a positive control identified 3 out of 5000 transcripts up-regulated in these cells (cyclooxygenase-1, tenascin-C, and TPA-1; Feng et al., 1999, *Circ. Res.* 85:1118-1123). Down-regulated genes included thrombomodulin and matrix metalloproteinase-1 (MMP). Recently, Zhang et al. (*Physiol. Genomics* 5: 187-192) utilized the cDNA microarray approach to ascertain gene expression profiles of human coronary artery VEC treated with nicotine. Their analysis of over 4,000 genes identified a number of nicotine-modulated genes involved in signal transduction and transcriptional regulation. Changes in gene expression profiles associated with endothelial senescence have been investigated using cDNA array hybridization with mRNA isolated from late vs. early passages of dermal VEC (Vasile et al., 2001, *FASEB* 15: 458-466). The study results suggest that the expression of thymosin beta-10, a G-sequestering peptide involved in actin regulation, was strongly down regulated in senescent endothelial cells.

US-PAT-NO: 6984517

DOCUMENT-IDENTIFIER: US 6984517 B1

TITLE: AAV5 vector and uses thereof

----- KWIC -----

Description Paragraph - DETX (24):

Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV5 vector can include, but are not limited to the following: nucleic acids encoding secretory and nonsecretory proteins, nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-P, and interferon-.gamma.; interleukins, such as IL-1, IL-1.beta., and ILs-2 through-14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; anit-HIV decoy tar elements; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Another target cell is the lung airway cell, which can be used to administer nucleic acids, such as those coding for the cystic fibrosis transmembrane receptor, which could provide a gene therapeutic treatment for cystic fibrosis. Other target cells include muscle cells where useful nucleic acids, such as those encoding cytokines and growth factors, can be transduced and the protein the nucleic acid encodes can be expressed and secreted to exert its effects on other cells, tissues and organs, such as the liver. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Description Paragraph - DETX (90):

The present invention provides recombinant vectors based on AAV5. Such vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulfate proteoglycans which is very inefficient with AAV2 based vectors. These vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some

examples of this type of treatment include, but are not limited to, the introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

US-PAT-NO: 6984379

DOCUMENT-IDENTIFIER: US 6984379 B1

TITLE: Gene therapy by administration of genetically engineered
CD34.sup.+ cells obtained from cord blood

----- KWIC -----

Brief Summary Text - BSTX (36):

Nucleic acid sequences encoding therapeutic agents which may be placed into the vector include, but are not limited to, nucleic acid sequences encoding cytokines, tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; the gamma chain of the IL-2 receptor; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; ZAP70 transcription factor; Fc receptors for antigen-binding domains of antibodies, the RAG1 and RAG2 genes, which encode enzymes that are essential for assembly of T-cell and B-cell receptors, and antisense sequences such as those that inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 6953842

DOCUMENT-IDENTIFIER: US 6953842 B2

TITLE: Antibodies to heregulin 2

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

US-PAT-NO: 6929955

DOCUMENT-IDENTIFIER: US 6929955 B2

TITLE: Interactive system for presenting and eliminating
substances

----- KWIC -----

Detailed Description Text - DETX (136):

Biocompatible tissue layers made from plastic materials onto which monodisperse PAMA particles had been adhered or copolymers having PAMA as a basic material are primed with organ-specific pegylated cellular growth factor. This allows a rapid and controlled coating of the organ substitute materials.

US-PAT-NO: 6919206

DOCUMENT-IDENTIFIER: US 6919206 B2

TITLE: Medium containing flt3 ligand for culturing
hematopoietic cells

----- KWIC -----

Claims Text - CLTX (2):

2. The hematopoietic cell expansion medium of claim 1, further comprising a cellular growth factor.

Claims Text - CLTX (10):

10. The method according to claim 9, further comprising contacting the cells with a cellular growth factor.

US-PAT-NO: 6905681

DOCUMENT-IDENTIFIER: US 6905681 B1

See image for Certificate of Correction

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Detailed Description Text - DETX (126):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 6905680

DOCUMENT-IDENTIFIER: US 6905680 B2

See image for Certificate of Correction

TITLE: Methods of treating HIV infected subjects

----- KWIC -----

Detailed Description Text - DETX (135):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0×10^6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5×10^6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0×10^6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 6887466

DOCUMENT-IDENTIFIER: US 6887466 B2

See image for Certificate of Correction

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Detailed Description Text - DETX (120):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 6864264

DOCUMENT-IDENTIFIER: US 6864264 B1

TITLE: 1-adamantyl chalcones for the treatment of proliferative disorders

----- KWIC -----

Detailed Description Text - DETX (112):

The compounds of the present invention were evaluated by comparing breast cancer cell lines MCF-7 (ER-positive) and MDA-MB435 (ER-negative) with noncancerous breast epithelial cells (MCF-10). Those compounds that showed a high level of antiproliferative activity against tested breast cancer cell lines, but not against normal breast epithelial cells were evaluated for in vitro mechanism of action by looking at their effects against cellular growth factors, Epidermal Growth Factor (EGF), and Transforming Growth Factor (TGF-alpha).

US-PAT-NO: 6864085

DOCUMENT-IDENTIFIER: US 6864085 B2

TITLE: Bovine immunodeficiency virus (BIV) based vectors

----- KWIC -----

Detailed Description Text - DETX (63):

Additionally the gene of interest may be selected from DNA sequences encoding tumor necrosis factor genes, such as TNF-.alpha.; genes encoding interferons such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and interleukins 2 through 14, in particular IL-2, IL-4, IL-6 and IL-10; genes encoding GM-CSF or G-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoA1 and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, the NDI-1 gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication. Antisense sequences are designed to bind RNA transcripts and thereby prevent cellular synthesis of a particular protein or prevent use of that RNA sequence by the cell.

US-PAT-NO: 6855314

DOCUMENT-IDENTIFIER: US 6855314 B1

TITLE: AAV5 vector for transducing brain cells and lung cells

----- KWIC -----

Detailed Description Text - DETX (12):

Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV5 vector can include, but are not limited to the following: nucleic acids encoding secretory and nonsecretory proteins, nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; interleukins, such as IL-1, IL-1.beta., and ILs -2 through -14; GM-CSF; adenosine deaminase; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; anti-apoptotic gene products; proteins promoting neuronal survival, such as growth factors and glutamate receptors; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; anti-HIV decoy tar elements; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Another target cell is the lung airway cell, which can be used to administer nucleic acids, such as those coding for the cystic fibrosis transmembrane receptor, which could provide a gene therapeutic treatment for cystic fibrosis. Other target cells include muscle cells where useful nucleic acids, such as those encoding cytokines and growth factors, can be transduced and the protein the nucleic acid encodes can be expressed and secreted to exert its effects on other cells, tissues and organs, such as the liver. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Detailed Description Text - DETX (89):

The present invention provides recombinant vectors based on AAV5. Such vectors may be useful for transducing erythroid progenitor cells or cells lacking heparin sulfate proteoglycans which is very inefficient with AAY2 based vectors. These vectors may also be useful for transducing cells with a nucleic acid of interest in order to produce cell lines that could be used to screen for agents that interact with the gene product of the nucleic acid of interest. In addition to transduction of other cell types, transduction of erythroid

cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some examples of this type of treatment include, but are not limited to, the introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

US-PAT-NO: 6849454

DOCUMENT-IDENTIFIER: US 6849454 B2

TITLE: Highly efficient gene transfer into human repopulating stem cells by RD114 pseudotyped retroviral vector particles

----- KWIC -----

Detailed Description Text - DETX (36):

According to the invention, the gene of interest carried by the RD114 can be any gene pseudotyped vector particle. In a preferred embodiment, the gene of interest is a therapeutically relevant gene. The non-limiting examples of such genes include genes encoding wild-type proteins missing in mutant cells (e.g., factors VII and IX, tumor suppressor genes, etc.) and genes involved in drug resistance or anti-viral resistance (e.g., MDR, ribozymes, antisense RNAs, anti-vital proteases, etc.). Examples of therapeutic genes include polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1 AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, e.g., the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; anti-tumor protein intracellular antibodies; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and

endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent. In one of the embodiments, the invention also discloses the use of a gene of interest encoding a marker gene, such as enhanced green fluorescent protein (EGFP). Such marker genes are particularly useful for tracking the fate of transduced cells, e.g., during clinical development of a gene therapy based on the vectors and methods of the invention.

US-PAT-NO: 6846628

DOCUMENT-IDENTIFIER: US 6846628 B1

TITLE: Selection methods

----- KWIC -----

Detailed Description Text - DETX (106):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detailed Description Text - DETX (110):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 6821511

DOCUMENT-IDENTIFIER: US 6821511 B2

TITLE: Methods of using adeno-associated virus rep protein

----- KWIC -----

Detailed Description Text - DETX (13):

DNA sequences encoding therapeutic agents which may be placed into the genetic construct include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha., interferons, such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1-B, and Interleukins 2 through 14; gene encoding GM-CSF; genes encoding adenosine deaminase or ADA; genes encoding cellular growth factors or cytokines, such as epithelial growth factor (EGF), keratinocyte growth factor (KGF), and lymphokines, which are growth factors for lymphocytes; gene encoding soluble CD4; Factor VII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI, and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; superoxide dismutase genes, such as Cu-SOD, Mn-SOD, and Zn-SOD; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus. Additional therapeutic agents include genetic transcripts such as a messenger RNA, antisense RNA, or ribozymes. It is to be understood, however, that the scope of the present invention is not intended to be limited to the specific therapeutic agents described hereinabove.

US-PAT-NO: 6808522

DOCUMENT-IDENTIFIER: US 6808522 B2

TITLE: Microchip devices for delivery of molecules and methods
of fabrication thereof

----- KWIC -----

Detailed Description Text - DETX (24):

A wide variety of molecules can be contained in and released from the microchip devices. Examples of the molecules include drugs, diagnostic reagents, fragrances, dyes or coloring agents, sweeteners and other flavoring agents, and compounds used in tissue culture, such as cellular growth factors.

US-PAT-NO: 6774227

DOCUMENT-IDENTIFIER: US 6774227 B1

See image for Certificate of Correction

TITLE: Therapeutic uses of factors which inhibit or neutralize
MIF activity

----- KWIC -----

Brief Summary Text - BSTX (10):

The invention is based, in part, on the Applicants' unexpected finding that MIF is required for the proliferation of T cells in vitro. Neutralizing monoclonal antibodies (mAbs) against MIF directly inhibited the proliferation of anti-CD3 induced primary T cells. These results suggest that MIF functions as a cellular growth factor and that MIF plays a role in regulating cellular proliferation.

US-PAT-NO: 6761884

DOCUMENT-IDENTIFIER: US 6761884 B1

TITLE: Vectors including foreign genes and negative selective
markers

----- KWIC -----

Brief Summary Text - BSTX (17):

Heterologous or foreign genes which may be placed into the vectors of the present invention include, but are not limited to genes which encode cytokines or cellular growth factors, such as lymphokines, which are growth factors for lymphocytes. Other examples of foreign genes include, but are not limited to, genes encoding soluble CD4, Factor VIII, Factor IX, ADA, the LDL receptor, ApoE, and ApoC.

US-PAT-NO: 6734289

DOCUMENT-IDENTIFIER: US 6734289 B2

See image for Certificate of Correction

TITLE: Gastrokines and derived peptides including inhibitors

----- KWIC -----

Abstract Text - ABTX (1):

A novel group of gastrokines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Control of mammalian gastro-intestinal tissues growth and repair is facilitated by the use of the proteins, making the proteins candidates for therapies.

Brief Summary Text - BSTX (2):

A novel group of Gastric Antrum Mucosal Proteins that are gastrokines, is characterized. A member of the gastrokine group is designated AMP-18. AMP-18 genomic DNA, and cDNA molecules are sequenced for human and mouse, and the protein sequences are predicted from the nucleotide sequences. The cDNA molecule for pig AMP-18 is sequenced and confirmed by partial sequencing of the natural protein. The AMP-18 protein and active peptides derived from its sequence are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein sequence. Control of mammalian gastro-intestinal tissues growth and repair is facilitated by the use of the protein or peptides, making the protein and the derived peptides candidates for therapies.

Brief Summary Text - BSTX (6):

A novel gene product designated Antrum Mucosal Protein 18 ("AMP-18") is a gastrokine. The protein was discovered in cells of the stomach antrum mucosa by analysis of cDNA clones obtained from humans, pigs, and mice. The protein is a member of a group of cellular growth factors or cytokines, more specifically gastrokines. The AMP-18 cDNA sequences predict a protein 185 amino acids in length for both pig and man. The nucleotide sequences also predict a 20-amino acid N-terminal signal sequence for secreted proteins. The cleavage of this N-terminal peptide from the precursor (preAMP-18) was confirmed for the pig protein; this cleavage yields a secreted protein 165 amino acids in length and ca.18,000 Daltons (18 kD) in size. Human and mouse genomic DNA sequences were also obtained and sequenced. A human genomic DNA was isolated in 4 overlapping fragments of sizes 1.6 kb, 3 kb, 3.3 kb and 1.1 kb respectively. The mouse genomic DNA sequence was isolated in a single BAC clone.

US-PAT-NO: 6703017

DOCUMENT-IDENTIFIER: US 6703017 B1

See image for Certificate of Correction

TITLE: Reversal of insulin-dependent diabetes by
islet-producing stem cells, islet progenitor cells and
islet-like structures

----- KWIC -----

Detailed Description Text - DETX (9):

The cell suspension prepared in the nutrient medium supplemented with normal serum and about 2.5-10 mM glucose is then incubated under conditions that facilitate cell growth, preferably at about 37.degree. C. and, preferably, in an atmosphere of about 5% CO.sub.2. This incubation period is, thus, carried out utilizing standard procedures well known to those skilled in the art. During this time ductal epithelial cells proliferate and establish a monolayer which will ultimately give rise to IPSCs. The initiation of cellular differentiation can be brought about by re-feeding the cultures with Click's EHAA or like medium supplemented with normal serum as discussed above. Rapid re-feeding was found to induce extensive IPC and IdI formation with considerable cell differentiation. We have found that cellular differentiation is further enhanced by inclusion of relatively high concentrations of glucose (about 10-25 mM and preferably 16.7 mM) in the re-feed medium. In addition, it is contemplated that any of a number of other biological factors, including but not limited to factors which up-regulate the Reg gene, such as hepatocyte growth/scatter factor, and other cellular growth factors, such as insulin-like-growth factor, epidermal growth factor, keratinocyte growth factor, fibroblast growth factor, nicotinamide, and other factors which modulate cellular growth and differentiation can be added to the cultures to optimize and control growth and differentiation of the IPSCs. By employing any of these various factors, or combinations thereof, at different stages, at different seeding densities and at different times from seeding in the course of IPSC differentiation, IPSC cultures are optimized. In addition, factors produced by the IPSC cultures in the course of differentiation which augment growth can be isolated, sequenced, cloned, produced in mass quantities, and added to IPSC cultures to facilitate growth and differentiation of those cultures. The relevant factors are identified by concentrating IPSC culture supernates from early, intermediate and late stages of differentiation and testing for the ability of these concentrates to augment IPSC growth and differentiation. Positive effects are correlated with molecular constituents in the concentrates by two-dimensional gel electrophoresis of positive and negative supemates, purification and N-terminal sequencing of spots present only in the positive concentrates and subsequent cloning and expression of the genes encoding these factors.

US-PAT-NO: 6689775

DOCUMENT-IDENTIFIER: US 6689775 B2

TITLE: Uses of thioredoxin

----- KWIC -----

Detailed Description Text - DETX (88):

4.6.2 Role of Oxidative Inactivation of Thioredoxin as a Cellular Growth Factor

US-PAT-NO: 6689351

DOCUMENT-IDENTIFIER: US 6689351 B1

See image for Certificate of Correction

TITLE: Use of GM-CSF to promote accelerated wound healing

----- KWIC -----

Brief Summary Text - BSTX (52):

Recombinant SCF is a novel cellular growth factor which stimulates the growth of early hematopoietic progenitor cells, neural stem cells, and primordial germ stem cells [PCT/US90/05548, filed Sep. 28, 1990]. SCF exhibits potent synergistic activities in conjunction with colony stimulating factors, resulting in increased numbers of colonies and colonies of greater size [Martin et al., (1990) Cell, vol. 63: 203-11]. Thus, administration of SCF to mammals in pharmacologic doses, alone or in combination with other colony stimulating factors or other hematopoietic growth factors, may lead to the improvement of damaged cells in a number of divergent organ systems.

US-PAT-NO: 6689161

DOCUMENT-IDENTIFIER: US 6689161 B2

TITLE: Decellularized vascular prostheses resistant to thrombus
occlusion and immunologic rejection

----- KWIC -----

Brief Summary Text - BSTX (32):

It is also an object of the present invention to provide a method of linking decellularized vascular tissue with at least one anti-thrombogenic agent and applying a second linking of at least one cellular growth factor so that the modified vascular tissue may be used as a vascular prosthesis.

US-PAT-NO: 6680306

DOCUMENT-IDENTIFIER: US 6680306 B2

See image for Certificate of Correction

TITLE: Method for enhancing the effectiveness of cancer
therapies

----- KWIC -----

Brief Summary Text - BSTX (7):

Galectin-1 is a highly conserved homodimer of 14-15 kD and is one of the most abundant of the galectins. It binds to laminin which has been found to exert strong regulatory effects on cellular interactions such as adhesion, proliferation, migration and differentiation. In this regard, galectin-1 has been found to strongly influence these processes in various cells. It is believed to be implicated in the secretion of a number of cellular growth factors and interleukins. Galectin-1 has been found to be expressed at very high levels in many cancer cells and is strongly implicated in metastasis.

US-PAT-NO: 6669683

DOCUMENT-IDENTIFIER: US 6669683 B2

TITLE: Thermally-activated microchip chemical delivery devices

----- KWIC -----

Brief Summary Text - BSTX (11):

The reservoirs can contain multiple drugs or other molecules in variable dosages. Each of the reservoirs of a single microchip can contain different molecules and/or different amounts and concentrations, which can be released independently. Examples of molecules to be delivered include drugs, fragrances, dyes or coloring agents, sweeteners, diagnostic reagents, and compounds used in tissue culture, such as cellular growth factors.

US-PAT-NO: 6656496

DOCUMENT-IDENTIFIER: US 6656496 B1

TITLE: Porous tissue scaffolding materials and uses thereof

----- KWIC -----

Brief Summary Text - BSTX (12):

Using natural biomaterials, such as fibrin and albumin, delivery of a biochemical agent can be accomplished in a number of different ways. For example, the fibrin or PEG crosslinked albumin can be impregnated with the biochemical factor or agent; the agent can be attached to the polymer chain or it can be included through intra-fibril entrapment. Certain growth factors like FGF can bind to these polymers, like fibrin, Otherwise, the growth factors need to be attached through various linkages. When the growth factor is bound, it is released only when the fibrin or albumin degrades. Since the degradation is cellular, the growth factor release is controlled by the rate of phagocytic cellular infiltration and is thus under biofeedback control. Additionally, the degradation is at the wound edge and thus gives the appropriate gradient to stimulate further angiogenesis and tissue healing.

US-PAT-NO: 6649375

DOCUMENT-IDENTIFIER: US 6649375 B2

TITLE: Adenoviral vectors for enhanced gene expression

----- KWIC -----

Detailed Description Text - DETX (35):

DNA sequences encoding therapeutic agents which may be placed into the adenoviral vector include, but are not limited to, DNA encoding Factor VIII and Factor IX as hereinabove described; DNA encoding cytokines; DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

Claims Text - CLTX (4):

4. The vector of claim 1, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (17):

17. The vector of claim 11, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA

encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (29):

29. The vector of claim 24, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (44):

44. The method of claim 39, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (57):

57. The vector of claim 54, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (70):

70. The vector of claim 64, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1

antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (82):

82. The vector of claim 77, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

Claims Text - CLTX (97):

97. The method of claim 92, wherein said heterologous DNA sequence is selected from the group consisting of: DNA encoding Factor VIII; DNA encoding Factor IX; DNA encoding a cytokine; DNA encoding a tumor necrosis factor (TNF); DNA encoding an interferon; DNA encoding an interleukin; DNA encoding GM-CSF; DNA encoding adenosine deaminase, or ADA; DNA encoding a cellular growth factor; DNA encoding soluble CD4; DNA encoding an LDL receptor; DNA encoding ApoE; DNA encoding ApoC; DNA encoding ApoA1; DNA encoding alpha-1 antitrypsin (.alpha.1AT); DNA encoding ornithine transcarbamylase (OTC); DNA encoding CFTR; DNA encoding insulin; DNA encoding a viral thymidine kinase; and DNA encoding an antisense sequence which inhibits viral replication.

US-PAT-NO: 6630442

DOCUMENT-IDENTIFIER: US 6630442 B1

TITLE: Reparatives for chemosurgery and laser (thermal) therapy

----- KWIC -----

Brief Summary Text - BSTX (44):

Certain antioxidants, particularly the endogenous L-glutathione and superoxide dismutase, as well as the element selenium, a co-factor for the enzyme glutathione peroxidase, and thiol compounds such as L-cysteine, can be employed in suitable carriers such as lotions, solutions, creams, ointments, foundation products, balms, sprays, aerosols or gels to protect and to treat the overlying skin surface in dealing specifically with the effects of the various free radicals on biornolecules, lipids, and cell membranes. Moreover, specific cellular growth factors, such as epithelial (epidermal) and/or fibroblast growth factors in appropriate concentrations and delivery vehicles, will be incorporated to these reparative preparations for accelerating healing of these wounds with quality repair.

US-PAT-NO: 6596924

DOCUMENT-IDENTIFIER: US 6596924 B1

See image for Certificate of Correction

TITLE: Graft animal model for high induction of papillomas, the
propagation of papillomavirus and evaluation of candidate
therapeutic agents

----- KWIC -----

Detailed Description Text - DETX (13):

The term "injuring" refers to any means of causing profound injury or wound to a tissue, which would result in tissue healing activity. Tissue injury can be induced by physical wounding or chemical damage. Non-limiting examples of physical wounding include: perforating, slitting, cutting, punching holes, burning and meshing using appropriate tools known in the art (e.g. scalpels, needles, pins, hole borers, meshers, etc.). Non-limiting examples of chemical damage include; enzymatic treatment and chemical burning. Tissue healing activity comprises new cell growth and increases in cellular growth factors and adhesion factors such as kinins and integrins. In addition, tissue healing activity may also be induced by other means such as electrical and chemical stimulation, chemical stimulation may include application of growth factors and/or enzymes to the tissue.

US-PAT-NO: 6596477

DOCUMENT-IDENTIFIER: US 6596477 B1

See image for Certificate of Correction

TITLE: Treatment and prevention of immunodeficiency virus
infection by administration of non-pyrogenic derivatives
of lipid A

----- KWIC -----

Detailed Description Text - DETX (65):

For example, the non-pyrogenic LPS or lipid A described herein may alone or in conjunction with a co-stimulatory factor (e.g. C-CSF, GM-CSF, a cytokine (e.g. an interleukin) or a cellular growth factor) can provide a less toxic method for activation of latent HIV-1 reservoirs (such as the latent infected cells that may remain after HAART or other anti-HIV therapeutic regimens (See Example 10).

US-PAT-NO: 6586002

DOCUMENT-IDENTIFIER: US 6586002 B2

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (5):

A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments, for use in active immunity; cytokines and cellular growth factors, for stimulating immunological inflammatory responses; hormones; and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, Philips, Waldmann).

Brief Summary Text - BSTX (12):

Preferred effectors include: (a) an antibody F.sub.ab fragment specific against a blood-circulating pathogen, for use in treating the subject for infection by the pathogen; (b) a CD4 glycoprotein, for use in treating the subject for infection by human immunodeficiency virus (HIV); (c) a cytokine or cellular growth factor, for use in stimulating an immune response in the subject; (d) a mono or polysaccharide, such as sialyl Lewis.sup.x, which binds to endothelial leukocyte adhesion molecule (ELAM), for use in treating a vascular inflammation related to neutrophil recruitment into sites of inflammation; (e) IL-1 inhibitor or IL-1RA, for treating the subject to achieve immune-response suppression; (f) polymyxin B, or polymyxin B decapeptide, for treating the subject for septic shock; and

Claims Text - CLTX (2):

2. The composition of claim 1 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (8):

8. The composition of claim 7 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (14):

14. The composition of clam 13 wherein the effector molecule is selected

from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (20):

20. The composition of claim 19 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (26):

26. The composition of claim 25 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (32):

32. The composition of claim 31 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (38):

38. The composition of claim 37 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

Claims Text - CLTX (44):

44. The composition of claim 43 wherein the effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF).

US-PAT-NO: 6562784

DOCUMENT-IDENTIFIER: US 6562784 B1

TITLE: Indications of mannan-binding lectin (MBL) in the
treatment of immunocompromised individuals

----- KWIC -----

Detailed Description Text - DETX (25):

Other biologic and immunomodulating agents have been used in treatment of patients with neutropenia and fever. Intravenous immunoglobulin has no benefit in preventing fever or infection in patients with neutropenia, but may have a moderate effect in patients with antibody deficiencies. Interferon gamma may add a benefit to patients with some neutrophil deficiencies, but this is not finally proven. Cellular growth factors (granulocyte and granulocyte-macrophage colony-stimulating factor) may shorten the duration of neutropenia and thus the need for antibiotics.

US-PAT-NO: 6562330

DOCUMENT-IDENTIFIER: US 6562330 B1

TITLE: Therapeutic use of polymers

----- KWIC -----

Brief Summary Text - BSTX (2):

The current chosen method for the treatment of aneurysms involves the packing of the aneurysm with platinum coils. Some work has been performed on the coating of these coils to provide a surface with increase thrombogenicity and render it biologically active by enabling the release of cellular growth factors and the like (German Patent DE-A-19647280). Others have concentrated on the use of polymer systems for embolising aneurysms, often simply by precipitating the polymer from a solution in a biocompatible solvent (WO-A-9745131). Specifically, a Japanese Group has had some success using a liquid composition containing a hardening polymer (cellulose acetate), with an X-ray contrast agent in a solvent such as DMSO. The polymer is caused to precipitate in-situ within the aneurysm when contacted with blood (JP-A-06-107549, J. Neurosurg., 83(3), 531, 1995). Another approach has been to directly polymerise monomers in-situ, an example of which is a iron-acrylic compound which polymerises rapidly and is non-toxic (J.Neurosurg., 47(2), 137, 1977). Yet another approach described in U.S. Pat. No. 5,749,894 is to introduce a coil and a polymeric composition which is melted by incident radiation and re-solidified in situ in the aneurysm. Examples of polymers are polyalkenes, poly(meth)acrylates, polyesters, polyamides and polysaccharides.

US-PAT-NO: 6552060

DOCUMENT-IDENTIFIER: US 6552060 B1

TITLE: Asymmetric disulfides and methods of using same

----- KWIC -----

Other Reference Publication - OREF (45):

Gasdaska, J.R. et al. Oxidative Inactivation of Thioredoxin as a Cellular Growth Factor and Protection by CYS(73).arrow-down dbl. Ser Mutation. Biochem. Pharmacol. 52 (1996): 1741-47.

US-PAT-NO: 6534055

DOCUMENT-IDENTIFIER: US 6534055 B1

See image for Certificate of Correction

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Detailed Description Text - DETX (124):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 6527762

DOCUMENT-IDENTIFIER: US 6527762 B1

See image for Certificate of Correction

TITLE: Thermally-activated microchip chemical delivery devices

----- KWIC -----

Brief Summary Text - BSTX (11):

The reservoirs can contain multiple drugs or other molecules in variable dosages. Each of the reservoirs of a single microchip can contain different molecules and/or different amounts and concentrations, which can be released independently. Examples of molecules to be delivered include drugs, fragrances, dyes or coloring agents, sweeteners, diagnostic reagents, and compounds used in tissue culture, such as cellular growth factors.

US-PAT-NO: 6514935

DOCUMENT-IDENTIFIER: US 6514935 B1

TITLE: Methods of treating hypertension

----- KWIC -----

Detailed Description Text - DETX (83):

The SmLIM/CRP2 promoter sequences of the invention may also be used in gene therapy to promote angiogenesis to treat diseases such as peripheral vascular disease or coronary artery disease. For example, the promoter sequences can be operably linked to heterologous sequences encoding cellular growth factors which promote angiogenesis, e.g., VEGF, acidic fibroblast growth factor, or basic fibroblast growth factor.

US-PAT-NO: 6506557

DOCUMENT-IDENTIFIER: US 6506557 B2

TITLE: Methods and compositions for identifying a protease

----- KWIC -----

Detailed Description Text - DETX (25):

One type of inhibitory protein binds to a receptor on the target cell. This type of inhibitory protein thus may include, but is not limited to, a single-chain antibody fragment to a hapten (Russell et al., Nucleic Acids Research 21(5), 1081-1085, 1993), CD3 or colonic carcinoma cell antigens (Ager et al., Human Gene Therapy 7(17), 2157-2164, 1996), or a cellular growth factors such as epidermal growth factor (EGF, Cosset et al., Journal of Virology 69(10), 6314-6322, 1995), stem cell factor (SCF, Fielding et al., Blood 91(5), 1802-9, 1998), and insulin-like growth factor I (IGF-I, Chadwick et al., J Mol Biol 285(2), 485-94, 1999).

US-PAT-NO: 6503752

DOCUMENT-IDENTIFIER: US 6503752 B1

TITLE: Lymphotropic agents and vectors

----- KWIC -----

Brief Summary Text - BSTX (5):

The following are references considered to be relevant for the subsequent description. 1. Salahuddin, S. Z., Ablashi, D. V., Markham, P. D., Josephs, S. F., Sturzenegger, S., Kaplan, M., Halligan, G., Biberfeld, P., Wong-Staal, F., Kramarsky, B., and Gallo, R. C. Isolation of a new virus, HBLV, in patients with lymphoproliferative disorders. *Science*, 234:596, 601, 1986. 2. Schirmer, E. C., Wyatt, L. S., Yamanishi, K., Rodriguez, W. J., and Frenkel, N. Differentiation between two distinct classes of viruses now classified as human herpesvirus 6. *Proc. Natl. Acad. Sci., USA*, 88:199-208, 1991. 3. Frenkel, N., Roffman, E., Schirmer, E. C., Katsafanas, G., Wyatt, L. S. and June, C. Cellular and growth factor requirements for the replication of human herpesvirus 6 in primary lymphocyte cultures, in: *Immunology and Prophylaxis of Human Herpesvirus Infections*, eds. Lopez, C., Mori, R., Roizman, B. and Whitley R. J., Plenum Publishing Corp. pp 1-8, 1990. 4. Kondo, K., Kondon, T., Okuno, T., Takahashi, M. and Yamanishi K. Human herpesvirus 6 infection of human monocytes/macrophages. *J. Gen. Virol.* 72:1401-1408, 1991. 5. Lusso, P., Ensoli, B., Markham, P. D., Ablashi, D. V., Salahuddin, S. Z., Tschachler, E., Wong-Staal, F., and Gallo, R. C. Production dual infection of human CD4.sup.+ lymphocytes by HIV-1 and HHV-6, *Nature*, 337:370-373, 1989. 6. Frenkel, N., Schirmer, E. C., Wyatt, L. S., Katsafanas, G., Roffman, E., Danovich, R. M., and June, C. H. Isolation of a new herpesvirus from human CD4.sup.+ T cells. *Proc. Natl. Acad. Sci., USA*, 87:748-752, 1990. 7. Wyatt, L. S., Rodriguez, W. J., Balachandran, N., and Frenkel, N. Human herpesvirus 7: antigenic properties and prevalence in children and adults. *J. Virol.*, 65:6260-6265, 1991. 8. Wyatt, L., and Frenkel, N. Human herpesvirus 7 is a constitutive inhabitant of adult human saliva. *J. Virol.* 66:3206-3209, 1992. 9. Pellett, P. E., Lindquister, G. J., Feorino, P., and Lopez, C. Genomic heterogeneity of human herpesvirus 6 isolates. *Adv. Exp. Med. Biol.* 278:9-18, 1990. 10. Lawrence, P. J., Chee, M., Craxton, M. A., Gompels, U. A., Honess, R. W., and Barrell, G. B. Human herpesvirus 6 is closely related to human cytomegalovirus. *J. Virol.* 64:287-299, 1990. 11. Lindquister, G. J., and Pellett, P. E. Properties of the human herpes-virus 6 strain Z29 genome: G+C content, length, and presence of variable-length directly repeated terminal sequence elements. *Virology.* 82:102-110, 1991. 12. Martin, M. E., Thomson, B. J., Honess, R. W., Craxton, M. A., Gompels, U. A., Liu, M. Y., Littler, E., Arrand, J. R., Teo, I., and Jones, M. D. The genome of human herpesvirus 6: maps of unit-length and concatemeric genomes for nine restriction endonucleases. *J. Gen. Virol.* 72:157-168, 1991b. 13. Frenkel, N., and Wyatt, L. S. Human herpesviruses 6 and 7 as exogenous agents in human

lymphocytes. Develop. Biol. Standard. 76:259-265, 1992. 14. Lopez, C., Pellett, P. Stewart, J., Coldsmith, C., Sanderlin, K., Black, J., Warfield, D. and Feorino, P. J. Infect. Dis., 157:1271-1273, 1988. 15. DiLuca, D., Katsafanas, G., Schirmer, E., Balachanran, N. and Frenkel, N. Virology, 175:199-210, 1990. 16. Frenkel, N., Schirmer, E. C., Wyatt, L. S., Katsafanas, G., Roffman, E., Danowich, R. M. and June, C. H. Proc. Natl. Acad. Sci., USA, 87:748-752, 1990.

Other Reference Publication - OREF (5):

Frenkel, Niza et al., "Cellular and Growth-Factor . . . Cultures," Plenum Publishing Corp., 1-8, 1990.

US-PAT-NO: 6503501

DOCUMENT-IDENTIFIER: US 6503501 B1

TITLE: Targetable vector particles

----- KWIC -----

Brief Summary Text - BSTX (40):

Thus, preferably, the vectors or vector particles of the present invention further include at least one heterologous gene. Heterologous or foreign genes which may be placed into the vector or vector particles include, but are not limited to, genes which encode cytokines or cellular growth factors, such as lymphokines, which are growth factors for lymphocytes. Other examples of foreign genes include, but are not limited to, genes encoding Factor VIII, Factor IX, tumor necrosis factors (TNF's), ADA, ApoE, ApoC, and Protein C.

US-PAT-NO: 6497876

DOCUMENT-IDENTIFIER: US 6497876 B1

TITLE: Method of stimulating an immune response with activated dendritic cells

----- KWIC -----

Detailed Description Text - DETX (7):

A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art. Briefly, ex vivo culture and expansion comprises: (1) collecting CD34^{sup}+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used.

US-PAT-NO: 6468524

DOCUMENT-IDENTIFIER: US 6468524 B1

See image for Certificate of Correction

TITLE: AAV4 vector and uses thereof

----- KWIC -----

Detailed Description Text - DETX (9):

Examples of heterologous nucleic acids which can be administered to a cell or subject as part of the present AAV4 vector can include, but are not limited to the following: nucleic acids encoding therapeutic agents, such as tumor necrosis factors (TNF), such as TNF-.alpha.; interferons, such as interferon-.alpha., interferon-.beta., and interferon-.gamma.; interleukins, such as IL-1, IL-1.beta., and ILs -2 through -14; GM-CSF; adenosine deaminase; secreted factors such as growth factors; ion channels; chemotherapeutics; lysosomal proteins; anti-apoptotic gene products; proteins promoting neural survival such as glutamate receptors and growth factors; cellular growth factors, such as lymphokines; soluble CD4; Factor VIII; Factor IX; T-cell receptors; LDL receptor; ApoE; ApoC; alpha-1 antitrypsin; ornithine transcarbamylase (OTC); cystic fibrosis transmembrane receptor (CFTR); insulin; Fc receptors for antigen binding domains of antibodies, such as immunoglobulins; and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A, non-B virus. The nucleic acid is chosen considering several factors, including the cell to be transfected. Where the target cell is a blood cell, for example, particularly useful nucleic acids to use are those which allow the blood cells to exert a therapeutic effect, such as a gene encoding a clotting factor for use in treatment of hemophilia. Furthermore, the nucleic acid can encode more than one gene product, limited only, if the nucleic acid is to be packaged in a capsid, by the size of nucleic acid that can be packaged.

Detailed Description Text - DETX (62):

The present invention provides recombinant vectors based on AAV4. Such vectors may be useful for transducing erythroid progenitor cells which is very inefficient with AAV2 based vectors. In addition to transduction of other cell types, transduction of erythroid cells would be useful for the treatment of cancer and genetic diseases which can be corrected by bone marrow transplants using matched donors. Some examples of this type of treatment include, but are not limited to, the introduction of a therapeutic gene such as genes encoding interferons, interleukins, tumor necrosis factors, adenosine deaminase, cellular growth factors such as lymphokines, blood coagulation factors such as factor VIII and IX, cholesterol metabolism uptake and transport protein such as EpoE and LDL receptor, and antisense sequences to inhibit viral replication of, for example, hepatitis or HIV.

US-PAT-NO: 6448390

DOCUMENT-IDENTIFIER: US 6448390 B1

TITLE: Stable envelope proteins for retroviral, viral and
liposome vectors and use in gene drug therapy

----- KWIC -----

Detailed Description Text - DETX (108):

The types of genes that are to be transferred into the host cell by the retrovirus particles of this invention may encode therapeutic agents, including, but not limited to, tumor necrosis factor genes (TNF); genes encoding interferons, such as interferon .alpha. (IFN-.alpha.); genes encoding interleukins (IL), such as IL-2 to IL-12; genes encoding granulocyte macrophage colony stimulating factor (GM-CSF); genes encoding adenosine deaminase (ADA); genes encoding cellular growth factors; genes encoding CD4, Factor VIII, Factor IX, T cell receptors, the LDL receptor, ApoE, ApoC, the .alpha.-1 antitrypsin gene, the ornithine transcarbamylase (OTC) gene, the DFTR gene, Fc receptors, and the insulin gene; antisense sequences which inhibit viral replication or replication of other genes; and genes encoding specific immunoglobulins or their fragments (Fv, scFv, Fab, Fab', or F(ab').sub.2). Further, these include, but are not limited to, suicide or lethal genes such as the gene encoding diphtheria toxin A-chain (Gelfand et al., U.S. Pat. No.4,830,962), Escherichia coli cytosine deaminase that renders cells susceptible to the drug 5-fluorocytosine (Ju et al., J Cancer Res Clin Oncol (1998) 124:683-689) or herpes simplex virus type-1 thymidine kinase that render cells susceptible to the drug gancyclovir (Fretag et al., Hum Gene Ther (1998) 9:1323-1333).

US-PAT-NO: 6429291

DOCUMENT-IDENTIFIER: US 6429291 B1

TITLE: Hyaluronan receptor protein

----- KWIC -----

Detailed Description Text - DETX (34):

Breast cancer is the most common malignant disease among women and represents a major cause of death in Western countries (Harris et al., 1992). Invasion and metastasis of the primary tumour remains the major cause of the fatal outcome of this particular malignancy (Price, 1990). Several cellular growth factors, cytokines, and oncogenes may play critical roles in the process of malignant transformation and progression in human breast cancer (Dickson et al., 1992).

US-PAT-NO: 6429001

DOCUMENT-IDENTIFIER: US 6429001 B1

TITLE: Recombinant AAV packaging systems

----- KWIC -----

Detailed Description Text - DETX (16):

In another aspect of the present invention the AAV vector particle-packaging cell also stably carries a second recombinant AAV genome consisting of AAV ITRs that flank a heterologous gene of interest. Suitable heterologous genes of interest include, but are not limited to DNA sequences encoding tumor necrosis factor (TNF), such as TNF-alpha, interferons such as Interferon-alpha, Interferon-beta, and Interferon-gamma, interleukins such as IL-1, II -1beta, and Interleukins 2 through 14, GM-CSF adenosine deaminase (ADA), cellular growth factors, such as lymphokines, soluble CD4, Factor VIII, Factor IX, T-cell receptors, the LDL receptor, ApoE, ApoC, alpha-1antitrypsin (alpha-1AT), ornithine transcarbamylase (OTC), CFTR, insulin, Fc receptors for antigen-binding domains of antibodies, and anti-sense sequences which inhibit viral replication, such as anti-sense sequences which inhibit replication of hepatitis B or hepatitis C virus.

US-PAT-NO: 6399746

DOCUMENT-IDENTIFIER: US 6399746 B1

See image for Certificate of Correction

TITLE: Structure, production and use of heregulin 2 ligands

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

US-PAT-NO: 6387686

DOCUMENT-IDENTIFIER: US 6387686 B2

TITLE: Methods and compositions for identifying a
polynucleotide encoding a protease

----- KWIC -----

Detailed Description Text - DETX (23):

One type of inhibitory protein binds to a receptor on the target cell. This type of inhibitory protein thus may include, but is not limited to, a single-chain antibody fragment to a hapten (Russell et al., Nucleic Acids Research 21(5), 1081-1085, 1993), CD3 or colonic carcinoma cell antigens (Ager et al., Human Gene Therapy 7(17), 2157-2164, 1996), or a cellular growth factors such as epidermal growth factor (EGF, Cosset et al., Journal of Virology 69(10), 6314-6322, 1995), stem cell factor (SCF, Fielding et al., Blood 91(5), 1802-9, 1998), and insulin-like growth factor I (IGF-I, Chadwick et al., J Mol Biol 285(2), 485-94, 1999).

US-PAT-NO: 6379959

DOCUMENT-IDENTIFIER: US 6379959 B1

See image for Certificate of Correction

TITLE: Metalocarboxypeptidase inhibitors and derived molecules
used as antitumor agents

----- KWIC -----

Brief Summary Text - BSTX (5):

A relevant structural feature of the PCI is that it is a small protein which contains a globular core stabilized by means of three disulfide bridges which constitute a cystine knot. We are referring to a topological pattern shared by other proteins, whether functionally related or not, which employ various cysteines concentrated in a central zone in order to create a stabilizing knot of disulfide bridges. This ensemble of proteins constitutes the so called group of knotins, because of the topological knot they form. We have to underline that, among the proteins which share this structural pattern with PCI, there are various cellular growth factors such as, for instance, the α and β -TGF, NGF, PDGF, EGF and those of the insulin family (Isaacs, N. (1995) Curr. Opin. Struct. Biol., 5:391-395; Lin, S et al. (1995) Nature Struct. Biol., 2, 835-837; Sun P. & Davies, D. (1995) Ann. Rev. Biophys. Biomol. Struct., 24: 269-291). In the specific case of the PCI, the globular core contains 27 amino acid residues and is flanked by two tails of 7 residues (the N-terminal tail) and of 5 residues (the C-terminal tail). The disulfide bridges are between cysteines 8-24, 12-27 and 18-34. This is the most frequent natural form, the so called IIa form, although there are other isoforms (Hass, G. M. & Ryan, C. A. (1981) Meth. Enzymol., 80: 778-791).

Brief Summary Text - BSTX (16):

Finally, another relevant point to take into consideration for the present invention is the structural analogy, topological, previously described between the PCI and the different cellular growth factors of the group of the knotins (Isaacs, N. (1995) Curr. Opin. Struct. Biol., 5: 391-395; Lin, S. et al. (1995) Nature Struct. Biol., 2: 835-837; Sun, P. & Davies, D. (1995) Ann. Rev. Biophys. Biomol. Struct., 24: 269-291). This analogy has made it possible to establish the hypothesis that the antitumoral activity of the PCI may be also totally or partially related to this knotin topology and not only to the protease inhibiting capacity. Thus, the PCI could act as an antagonist of growth factors and would block tumoral growth. As regards this aspect, it deserves to be mentioned that it has been reported that monoclonal antibodies against EGF interacting with heparin block the growth in vitro of some tumors and, therefore, could be used as therapeutic agents (Modjtahedi, H. & Dean, C. (1995) Biochim. Biophys. Res. Commun., 207: 389-397). In the same way, monoclonal antibodies or antisense RNA or genetic ablation or creation of dominant-negative mutants of the IGF-IR have been found to inhibit various

types of tumors (for a review, see Baserga, R. (1996) TIBTECH, 14: 150-152).

US-PAT-NO: 6372772

DOCUMENT-IDENTIFIER: US 6372772 B1

TITLE: Inhibitors of redox signaling and methods of using same

----- KWIC -----

Other Reference Publication - OREF (56):

Gasdaska, J.R. et al. Oxidative Inactivation of Thioredoxin as a Cellular Growth Factor and Protection by CYS(73). Ser Mutation. Biochem. Pharmacol. 52 (1996): 1741-47.

US-PAT-NO: 6352694

DOCUMENT-IDENTIFIER: US 6352694 B1

See image for Certificate of Correction

TITLE: Methods for inducing a population of T cells to proliferate using agents which recognize TCR/CD3 and ligands which stimulate an accessory molecule on the surface of the T cells

----- KWIC -----

Detailed Description Text - DETX (139):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 6342390

DOCUMENT-IDENTIFIER: US 6342390 B1

TITLE: Lipid vesicles containing adeno-associated virus rep
protein for transgene integration and gene therapy

----- KWIC -----

Detailed Description Text - DETX (13):

DNA sequences encoding therapeutic agents which may be placed into the genetic construct include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha., interferons, such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1-B, and Interleukins 2 through 14; gene encoding GM-CSF; genes encoding adenosine deaminase or ADA; genes encoding cellular growth factors or cytokines, such as epithelial growth factor (EGF), keratinocyte growth factor (KGF), and lymphokines, which are growth factors for lymphocytes; gene encoding soluble CD4; Factor VII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI, and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase gene, the CFTR gene, the insulin gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; superoxide dismutase genes, such as Cu-SOD, Mn-SOD, and Zn-SOD; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus. Additional therapeutic agents include genetic transcripts such as a messenger RNA, antisense RNA, or ribozymes. It is to be understood, however, that the scope of the present invention is not intended to be limited to the specific therapeutic agents described hereinabove.

US-PAT-NO: 6337320

DOCUMENT-IDENTIFIER: US 6337320 B1

TITLE: Reparatives for ultraviolet radiation skin damage

----- KWIC -----

Brief Summary Text - BSTX (39):

Certain antioxidants, particularly the endogenous L-glutathione, superoxide dismutase and acetyl L carnitine, as well as the element selenium, a co-factor for the enzyme glutathione peroxidase, and thiol compounds such as L-cysteine, can be employed in suitable carriers such as lotions, solutions, creams, ointments, balms, sprays, aerosols, gels or foundation compositions to protect and to treat the overlying skin surface as a result of the putative acute and chronic UV radiation etiologic factors in specifically dealing with the effects of the various free radicals on biomolecules, lipids, and cell membranes. Moreover, specific cellular growth factors, such as epithelial and fibroblast growth factors in appropriate concentrations and delivery vehicles, are incorporated in the preventive and reparative preparations of this invention for aiding the repair of UV radiation damage of skin and healing of the superficial wounds as occurs in sunburns and in the chronic UV radiation injury known as photoaging of the skin.

Detailed Description Text - DETX (50):

Thus, sunburn should be treated with the combination of synergistic endogenous and exogenous antioxidants as outlined herein. Local anesthetics such as benzocaine and related caines may be added to ameliorate discomfort and pain, and tissue respiratory factor, which also diminishes sunburn pain and stimulates fibroblast's metabolic functions to deposit collagen. Also, to enhance the healing of skin, the present invention employs epidermal growth factor and/or other cellular growth factors and hormones, which stimulate epithelial cell growth, vital in the epidermis repair process, to accelerate wound healing. In addition, as noted, lipid peroxidation may be started in the lipid rich skin, as evidenced by metabolic products of peroxidation being assayed from both the burned skin as well as from distant organs to the site(s) of solar injury, especially in lung tissue. This is to be expected as cutaneous vascular injury occurs, releasing the enzyme xanthine oxidase which is present in abundant quantities in vascular endothelium. A drop in blood flow resulting in local hypoxia after the burn may trigger the conversion of the enzyme xanthine dehydrogenase to xanthine oxidase with the resulting production of free oxygen radical and hydrogen peroxide. Thus, the importance of providing chain breaking antioxidants locally for amelioration of lipid peroxidation and the concomitant cellular and tissue damage produced by the free radicals of lipid peroxidation.

US-PAT-NO: 6329199

DOCUMENT-IDENTIFIER: US 6329199 B1

TITLE: Retroviral vectors produced by producer cell lines
resistant to lysis by human serum

----- KWIC -----

Detailed Description Text - DETX (19):

Polynucleotides encoding therapeutic agents which may be contained in the retroviral plasmid vector include, but are not limited to, polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any

particular therapeutic agent.

US-PAT-NO: 6326353

DOCUMENT-IDENTIFIER: US 6326353 B1

See image for Certificate of Correction

TITLE: Enhanced circulation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (42):

A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments, for use in active immunity; cytokines and cellular growth factors, for stimulating immunological inflammatory responses; hormones; and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, Philips, Waldmann).

Brief Summary Text - BSTX (52):

(c) a cytokine or cellular growth factor, for use in stimulating an immune response in the subject;

US-PAT-NO: 6312421

DOCUMENT-IDENTIFIER: US 6312421 B1

TITLE: Aneurysm embolization material and device

----- KWIC -----

Detailed Description Text - DETX (12):

Some embodiments of the polymer sleeve or coil 60 or string comprise a foam component. These embodiments also include cellular growth factors, genes, gene products and drugs within the foam or as a coating on the foam. These embodiments promote healing and repair of the aneurysm.

US-PAT-NO: 6291661

DOCUMENT-IDENTIFIER: US 6291661 B1

See image for Certificate of Correction

TITLE: flt3-L mutants and method of use

----- KWIC -----

Detailed Description Text - DETX (51):

A procedure for "ex vivo expansion" of hematopoietic stem and progenitor cells is described in detail in U.S. Pat. No. 5,199,942. Briefly, the method includes the steps of collecting CD34.sup.+ hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants and expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3, or c-kit ligand can be used.

US-PAT-NO: 6258557

DOCUMENT-IDENTIFIER: US 6258557 B1

See image for Certificate of Correction

TITLE: Smooth muscle cell LIM promoter

----- KWIC -----

Detailed Description Text - DETX (63):

The SmLIM/CRP2 promoter sequences of the invention may also be used in gene therapy to promote angiogenesis to treat diseases such as peripheral vascular disease or coronary artery disease. For example, the promoter sequences can be operably linked to heterologous sequences encoding cellular growth factors which promote angiogenesis, e.g., VEGF, acidic fibroblast growth factor, or basic fibroblast growth factor.

US-PAT-NO: 6242236

DOCUMENT-IDENTIFIER: US 6242236 B1

TITLE: Method of promoting enzyme diversity

----- KWIC -----

Brief Summary Text - BSTX (8):

Recently, however, selection methods have been used to produce catalytic antibodies (see Smiley et al., "Selection of catalytic antibodies for a biosynthetic reaction from a combinatorial cDNA library by complementation of an auxotrophic Escherichia coli: antibodies for orotate decarboxylation," 91(18) Proceedings of the National Academy of Sciences of the United States of America 8319-23(1994), which is incorporated herein by reference; Janda et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries," 91(7) Proceedings of the National Academy of Sciences of the United States of America 2532-6), which is incorporated herein by reference. Such methods use selection pressure to isolate antibodies with desired properties instead of the more laborious screening techniques. For example, a catalytic antibody which catalyzes the formation of a cellular growth factor may be selected for in a cell auxotrophic for such growth factor.

US-PAT-NO: 6242010

DOCUMENT-IDENTIFIER: US 6242010 B1

TITLE: Synergistic antioxidant compositions in management of hemorrhoids and other ano-rectal inflammatory conditions

----- KWIC -----

Brief Summary Text - BSTX (2):

The present invention deals with compositions for ano-rectal inflammatory processes, hemorrhoidal syndromes, pruritus ani and ano-rectal wounds comprising a complex of synergistic antioxidants, including enzymatic co-factors, thiol and selenium compounds, zinc salts and cellular growth factors to decrease the local inflammatory response, abolish symptoms, and to promote wound healing and surgical repairs, such as post-hemorrhoidectomies, fistulectomies, and fissurectomies. These active ingredients will be administered using topical ano-genital and intra-rectal preparations, most particularly, ointments, salves, lotions, creams, patches, aerosols, sprays and others and as suppositories and foams for internal hemorrhoids and rectal inflammatory conditions so that the antioxidants neutralize and scavenge the free radicals generated in ano-rectal diseases and local wounds thereby reducing the pain, inflammation, swelling, itching, and tenderness in these anatomical parts, and together with other optional ingredients promote repair and healing.

Brief Summary Text - BSTX (20):

Local anesthetics such as benzocaine and related caines may be added to ameliorate discomfort and pain, and tissue respiratory factor, which also diminishes discomfort and stimulates fibroblast's metabolic functions to deposit collagen. As noted below, to enhance the healing of muco-cutaneous lesions, the present invention may also optionally add epidermal growth factor and/or other cellular growth factors and hormones, which stimulate epithelial cell growth, vital in the repair process to accelerate wound healing.

US-PAT-NO: 6191106

DOCUMENT-IDENTIFIER: US 6191106 B1

TITLE: Muteins of epidermal growth factor exhibiting enhanced
binding at low pH

----- KWIC -----

Brief Summary Text - BSTX (3):

This invention relates to the molecular biology of cellular growth factors and recombinant DNA technology. More specifically, this invention relates to epidermal growth factor (EGF) modified to increase its binding activity at low pH, and the therapeutic uses of modified EGF of the invention.

US-PAT-NO: 6180134

DOCUMENT-IDENTIFIER: US 6180134 B1

See image for Certificate of Correction

TITLE: Enhanced ciruculation effector composition and method

----- KWIC -----

Brief Summary Text - BSTX (40):

A number of emerging or current therapies involve intravenous injection of small (less than 50 Kdaltons) protein, polypeptide or polysaccharide effectors. Such effectors can include F.sub.ab antibody fragments for use in active immunity, cytokines and cellular growth factors for stimulating immunological inflammatory responses, hormones, and polysaccharides, which are capable of interacting with endothelial cell receptors to competitively block neutrophil binding to activated endothelial cells lining the blood vessel (Katre, et al.; Philips, et al.; Waldmann).

Brief Summary Text - BSTX (50):

(c) a cytokine or a cellular growth factor, for use in stimulating an immune response in the subject;

US-PAT-NO: 6162640

DOCUMENT-IDENTIFIER: US 6162640 A

See image for Certificate of Correction

TITLE: Selection methods

----- KWIC -----

Detailed Description Text - DETX (107):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detailed Description Text - DETX (111):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 6156497

DOCUMENT-IDENTIFIER: US 6156497 A

TITLE: Recombinase-mediated generation of adenoviral vectors

----- KWIC -----

Detailed Description Text - DETX (28):

DNA sequences encoding therapeutic agents which may be contained in the first polynucleotide, such as a plasmid as hereinabove described, from which the adenoviral vector is generated include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper--zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; DNA sequences encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be

limited to any particular therapeutic agent.

US-PAT-NO: 6087177

DOCUMENT-IDENTIFIER: US 6087177 A

TITLE: Selection methods

----- KWIC -----

Detailed Description Text - DETX (109):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detailed Description Text - DETX (113):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 6066499

DOCUMENT-IDENTIFIER: US 6066499 A

TITLE: Selection methods

----- KWIC -----

Detailed Description Text - DETX (110):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detailed Description Text - DETX (114):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down-modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 6057427

DOCUMENT-IDENTIFIER: US 6057427 A

TITLE: Antibody to cytokine response gene 2(CR2) polypeptide

----- KWIC -----

Brief Summary Text - BSTX (9):

This invention pertains to complementary deoxyribonucleic acid (cDNA) libraries enriched in clones containing genes induced by ligand stimulation of a cell having a corresponding receptor for the ligand, and to methods of producing the same. This invention also relates to the genes which are expressed immediately or early on as a consequence of such a ligand-receptor interaction, and to methods of identifying these genes. In accordance with the method of the invention, a cDNA library highly enriched in ligand-inducible genes is produced by activating a cellular receptor with a ligand to induce the expression of genes as a result of ligand-receptor binding, reverse transcribing these RNA, and differentially probing the cDNA and selecting clones that bind to induced cDNA, but not to uninduced cDNA. Useful ligands include any of those which can activate a specific cellular receptor, including natural or synthetic ligands for the receptor, e.g., cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Brief Summary Text - BSTX (19):

The method of the invention may be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors may be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides, among other types of receptors. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones) are useful as activators of certain cellular receptors. The ligand used to activate the receptor may be the natural ligand recognized by the receptor or a synthetic analogue or fragment. Alternatively, an antibody specific for the receptor and capable of activating the receptor may also be used. The receptor is, thus, activated by a ligand or other means of activation for a predetermined length of time and at an effective concentration. This activation may be carried out in the presence of labeled RNA precursors which are incorporated into the RNA synthesized by the cell in response to receptor activation. Thus, the RNA transcribed is labeled so as to be distinguished from preexisting RNA which is not labeled. Some labels (such as radiolabels) may be employed to monitor the newly synthesized RNA. Useful radiolabeled RNA precursors for such purposes include [³H]-uridine.

Other labels may be used to separate newly transcribed RNA from unlabeled RNA. For example, RNA synthesized from thiol-labeled RNA precursors specifically adheres to phenylmercury agarose (Woodford et al., *Anal. Biochem.* 178:166-172 (1988)). RNA newly synthesized in response to receptor activation may be separated from preexisting RNA in the cells. All RNA molecules expressed prior to ligand-activation pass through the phenylmethyl mercury column, leaving only the newly synthesized, thiol-(SH-) labeled RNA attached to the agarose via a covalent bond between the mercury and sulfur. The thiolabeled RNA molecules may then be eluted from the column by reducing the Hg-S bond with an excess of 2-mercaptoethanol. To augment the expression of immediate/early ligand-activated genes, which may be difficult to identify because of the large number of constitutively expressed genes, a substance that enhances the level of RNA may be added to the culture medium during the ligand stimulation (see, e.g., Cochran et al., *Cell* 33:939-947 (1983)). Useful substances include those compounds that stabilize RNA and/or that block translation, thereby blocking feedback inhibition of these genes by a later gene product. Such activity may potentiate the magnitude of the RNA expressed as well as the duration of the life of the RNA. Examples of such useful substances include cycloheximide (CHX), which inhibits protein synthesis at the level of RNA-ribosome complexing and may stabilize polysomal RNA, and puromycin, which inhibits translation by causing premature dissociation of the peptide-mRNA-ribosome complex. The labeled RNA transcribed consequent to receptor activation in the presence of the substance which enhances RNA levels may then be purified from the cytoplasm of the cells. The purification may be accomplished by extracting total cellular RNA from a cell homogenate or fraction thereof, isolating mRNA therefrom, for example, using a poly U or poly [dT] column, and then separating the labeled RNA from the unlabeled RNA. The separation may be accomplished, for example, using the phenylmethyl mercury agarose protocol described above. Of course, other known methods of separating the newly synthesized RNA from the preexisting can also be used.

US-PAT-NO: 6054281

DOCUMENT-IDENTIFIER: US 6054281 A

TITLE: Binding assays

----- KWIC -----

Brief Summary Text - BSTX (14):

A general method has been disclosed that allows the display of a polypeptide ligand (which may be glycosylated) on the surface of a retroviral vector as a genetically encoded extension of the viral envelope protein (WO94/06920, Medical Research Council). The engineered retroviral vector then adopts the binding specificity of the displayed ligand. To date several different polypeptide ligands have been displayed on murine leukaemia virus (MLV)-based retroviral vectors, including single chain antibodies, cellular growth factors and immunoglobulin binding domains (WO94/06920 Medical Research Council; Cosset et al., 1994 Gene Therapy 1 pS1; Nilson et al., 1994 Gene Therapy 1, pS17). In principle, this technology should allow the display of many different structural classes of binding domains on retroviral vectors, including glycopolypeptides and glycoproteins.

US-PAT-NO: 6051549

DOCUMENT-IDENTIFIER: US 6051549 A

TITLE: Heparin and sulfatide binding peptides from the type-I repeats of human thrombospondin and conjugates thereof

----- KWIC -----

Brief Summary Text - BSTX (11):

Heparin binding is critical for activities associated with many cellular growth factors, cell adhesion molecules, and certain enzymes involved in the blood clotting cascade. Agents to inhibit these interactions have found numerous uses in prevention of thrombosis. Heparin analogues have been shown to have anti-tumor and antimetastatic activities.

US-PAT-NO: 6051398

DOCUMENT-IDENTIFIER: US 6051398 A

See image for Certificate of Correction

TITLE: Nucleic acids encoding CR3 polypeptide, vector and transformed cell thereof, and expression thereof

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 6043093

DOCUMENT-IDENTIFIER: US 6043093 A

TITLE: Selection methods

----- KWIC -----

Detailed Description Text - DETX (107):

Positive cellular selection may occur in a variety of ways. In one example a cellular growth factor which confers a growth advantage to the cell is functionally down-modulated. The down-modulated cellular growth factor is complexed in a selection molecule so that upon production of the desired novel molecule the growth factor is functionally up-modulated. Thus selection of the desired novel molecule occurs through positive cellular selection.

Detailed Description Text - DETX (111):

Negative cellular selection may occur in a variety of ways. A cellular growth factor which confers a growth advantage on the cell has its function maintained or up-modulated when complexed in a selection molecule. Upon production of the desired novel molecule and the interaction of same with the selection molecule, the growth factor is functionally down- modulated. Thus selection of the desired novel molecule occurs through negative cellular selection.

US-PAT-NO: 6027914

DOCUMENT-IDENTIFIER: US 6027914 A

See image for Certificate of Correction

TITLE: Nucleic acids encoding CR6 polypeptide vector and transformed cell thereof, and expression thereof

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 6020155

DOCUMENT-IDENTIFIER: US 6020155 A

See image for Certificate of Correction

TITLE: Nucleic acids encoding CR1 fusion protein, vector,
transfected cell and expression

----- KWIC -----

Brief Summary Text - BSTX (10):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 6017527

DOCUMENT-IDENTIFIER: US 6017527 A

TITLE: Activated dendritic cells and methods for their
activation

----- KWIC -----

Detailed Description Text - DETX (7):

A procedure for ex vivo expansion of hematopoietic stem and progenitor cells is described in U.S. Pat. No. 5,199,942, incorporated herein by reference. Other suitable methods are known in the art. Briefly, ex vivo culture and expansion comprises: (1) collecting CD.sup.34 + hematopoietic stem and progenitor cells from a patient from peripheral blood harvest or bone marrow explants; and (2) expanding such cells ex vivo. In addition to the cellular growth factors described in U.S. Pat. No. 5,199,942, other factors such as flt3-L, IL-1, IL-3 and c-kit ligand, can be used.

US-PAT-NO: 6004798

DOCUMENT-IDENTIFIER: US 6004798 A

TITLE: Retroviral envelopes having modified hypervariable
polyproline regions

----- KWIC -----

Detailed Description Text - DETX (24):

Polynucleotides encoding therapeutic agents which may be contained in the retroviral vector particle include, but are not limited to, polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; anticoagulants; anti-platelet agents; anti-inflammatory agents; the erythropoietin gene; genes encoding G-CSF, GM-CSF, TGF-.alpha., TGF-.beta., and fibroblast growth factor; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; gene encoding clotting factors, including Factor VIII, Factor IX, protein S, protein C, antithrombin III, and von Willebrand Factor; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the cystic fibrosis transmembrane conductance regulator (CFTR) gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; polynucleotides encoding cell cycle control agents, agents which inhibit cyclin proteins, such as antisense polynucleotides to the cyclin G1 and cyclin D1 genes; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell

antigen receptor; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

US-PAT-NO: 6001647

DOCUMENT-IDENTIFIER: US 6001647 A

See image for Certificate of Correction

TITLE: In vitro growth of functional islets of Langerhans and
in vivo uses thereof

----- KWIC -----

Detailed Description Text - DETX (9):

The cell suspension prepared in the nutrient medium supplemented with normal serum and about 2.5-10 mM glucose is then incubated under conditions that facilitate cell growth, preferably at about 35-40.degree. C. and, preferably, in an atmosphere of about 5% CO.sub.2. This incubation period is, thus, carried out utilizing standard procedures well known to those skilled in the art. During this time stromal or ductal epithelial cells proliferate and establish a monolayer which will ultimately give rise to islet-like structures. The initiation of cellular differentiation can be brought about by re-feeding the cultures with Click's EHAA or like medium supplemented with normal serum as discussed above. Rapid re-feeding was found to induce extensive islet foci and islet-like structure formation with considerable cell differentiation. We have found that cellular differentiation is further enhanced by inclusion of relatively high concentrations of glucose (about 10-25 mM and preferably 16.7 mM) in the re-feed medium. In addition, it is contemplated that any of a number of other biological factors, including but not limited to factors which up-regulate the Reg gene, such as hepatocyte growth/scatter factor, and other cellular growth factors, such as insulin-like-growth factor, epidermal growth factor, keratinocyte growth factor, fibroblast growth factor, nicotinamide, and other factors which modulate cellular growth and differentiation can be added to the cultures to optimize and control growth and differentiation of the IPSCs. By employing any of these various factors, or combinations thereof, at different stages, at different seeding densities and at different times from seeding in the course of IPSC differentiation, IPSC cultures are optimized. In addition, factors produced by the IPSC cultures in the course of differentiation which augment growth can be isolated, sequenced, cloned, produced in mass quantities, and added to IPSC cultures to facilitate growth and differentiation of those cultures. The relevant factors are identified by concentrating IPSC culture supernates from early, intermediate and late stages of differentiation and testing for the ability of these concentrates to augment IPSC growth and differentiation. Positive effects are correlated with molecular constituents in the concentrates by two-dimensional gel electrophoresis of positive and negative supernates, purification and N-terminal sequencing of spots present only in the positive concentrates and subsequent cloning and expression of the genes encoding these factors.

US-PAT-NO: 5990088

DOCUMENT-IDENTIFIER: US 5990088 A

TITLE: Method for treating kaposi's sarcoma with antisense
oligonucleotides

----- KWIC -----

Brief Summary Text - BSTX (12):

A great deal of time, money, and effort has been invested in strategies to block the proliferative effects of cellular growth factors. Major resources have been invested into strategies for making antisense oligonucleotides to such growth factors in an effort to block their proliferative activities. In one experiment in vitro Kaposi's sarcoma cells were treated with antisense oligonucleotides against the cytokine IL-6. See Miles et al. Proc. Nat. Acad. Sci. USA 87:4068-4072 (1990) (embodied in International Patent Application No.: PCT/US92/04509, Publication No.: WO 92/21380 (the "Miles Application")). In the references, IL-6 was suggested to be the autocrine factor primarily responsible for proliferation of Kaposi's sarcoma cells. See Miles Application at p. 4, lines 29-33. However, IL-6 has not been shown to possess the angiogenic properties necessary for the full proliferation of Kaposi's sarcoma. Moreover, the reference indicates that relatively high dosages of antisense oligonucleotides are necessary to block the IL-6 induced proliferation of Kaposi's sarcoma. Miles Application at p. 4, lines 17-22.

US-PAT-NO: 5985655

DOCUMENT-IDENTIFIER: US 5985655 A

TITLE: Targetable vector particles

----- KWIC -----

Brief Summary Text - BSTX (41):

Thus, preferably, the vectors or vector particles of the present invention further include at least one heterologous gene. Heterologous or foreign genes which may be placed into the vector or vector particles include, but are not limited to, genes which encode cytokines or cellular growth factors, such as lymphokines, which are growth factors for lymphocytes. Other examples of foreign genes include, but are not limited to, genes encoding Factor VIII, Factor IX, tumor necrosis factors (TNF's), ADA, ApoE, ApoC, and Protein C.

US-PAT-NO: 5952225

DOCUMENT-IDENTIFIER: US 5952225 A

TITLE: Retroviral vectors produced by producer cell lines
resistant to lysis by human serum

----- KWIC -----

Detailed Description Text - DETX (19):

Polynucleotides encoding therapeutic agents which may be contained in the retroviral plasmid vector include, but are not limited to, polynucleotides encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; the CFTR gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myc oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .beta.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the LDL receptor; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; polynucleotides encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and polynucleotides encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any

particular therapeutic agent.

US-PAT-NO: 5951973

DOCUMENT-IDENTIFIER: US 5951973 A

TITLE: Use of interleukin-4 (IL-4) to treat rheumatoid
arthritis

----- KWIC -----

Brief Summary Text - BSTX (5):

This technology has progressed extremely rapidly in recent years and a variety of exogenous proteins have been expressed in a variety of hosts, but obtaining any desired novel cDNA clone remains an uncertainty. By way of example, some of the eukaryotic proteins produced by recombinant DNA technology include: proinsulin (Naber, S. et al., Gene 21:95-104 [1983]); interferons (Simon, L. et al., Proc. Natl. Acad. Sci. U.S.A., 80:2059-2062 [1983] and Derynck, R. et al., Nucl. Acids Res. 1:1819-1837 [1983]); growth hormone (Goeddel, D., et al., Nature 281:544-548 [1979]); a human T-cell growth factor (Taniguichi, T. et al., Nature 302:305-310 (1983)); and a granulocyte/macrophage cellular growth factor (G/M-CSF) (Miyatake, S. et al., EMBO J. 4:2561-2568 (1985)). These publications and other reference materials cited hereafter have been included to provide additional details on the background of the pertinent art and, in particular instances, the practice of the invention, and are all incorporated herein by reference.)

US-PAT-NO: 5935935

DOCUMENT-IDENTIFIER: US 5935935 A

TITLE: Adenoviral vectors for treatment of hemophilia

----- KWIC -----

Detailed Description Text - DETX (35):

DNA sequences encoding therapeutic agents which may be placed into the adenoviral vector include, but are not limited to, DNA encoding Factor VIII and Factor IX as hereinabove described; DNA encoding cytokines; DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 5925345

DOCUMENT-IDENTIFIER: US 5925345 A

TITLE: Vectors including foreign genes and negative selective
markers

----- KWIC -----

Brief Summary Text - BSTX (17):

Heterologous or foreign genes which may be placed into the vectors of the present invention include, but are not limited to genes which encode cytokines or cellular growth factors, such as lymphokines, which are growth factors for lymphocytes. Other examples of foreign genes include, but are not limited to, genes encoding soluble CD4, Factor VIII, Factor IX, ADA, the LDL receptor, ApoE, and ApoC.

US-PAT-NO: 5922584

DOCUMENT-IDENTIFIER: US 5922584 A

TITLE: Method for promoting enzyme diversity

----- KWIC -----

Brief Summary Text - BSTX (8):

Recently, however, selection methods have been used to produce catalytic antibodies (see Smiley et al., "Selection of catalytic antibodies for a biosynthetic reaction from a combinatorial cDNA library by complementation of an auxotrophic Escherichia coli: antibodies for orotate decarboxylation," 91(18) Proceedings of the National Academy of Sciences of the United States of America 8319-23(1994), which is incorporated herein by reference; Janda et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries," 91(7) Proceedings of the National Academy of Sciences of the United States of America 2532-6), which is incorporated herein by reference. Such methods use selection pressure to isolate antibodies with desired properties instead of the more laborious screening techniques. For example, a catalytic antibody which catalyzes the formation of a cellular growth factor may be selected for in a cell auxotrophic for such growth factor.

US-PAT-NO: 5922315

DOCUMENT-IDENTIFIER: US 5922315 A

TITLE: Adenoviruses having altered hexon proteins

----- KWIC -----

Detailed Description Text - DETX (11):

DNA sequences encoding therapeutic agents include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-A; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-T; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding ornithine transcarbamylase, or OTC; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; cytochrome b; glucocerebrosidase; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (alAT) gene; the insulin gene; the hypoxanthine phosphoribosyl transferase gene; negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myb oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; the phenylalanine hydroxylase gene; nitric oxide synthetase; vasoactive peptides; angiogenic peptides; the dopamine gene; the dystrophin gene; the .alpha.-globin gene; the .alpha.-globin gene; the HbA gene; protooncogenes such as the ras, src, and bcl genes; tumor-suppressor genes such as p53 and Rb; the heregulin-.alpha. protein gene, for treating breast, ovarian, gastric and endometrial cancers; monoclonal antibodies specific to epitopes contained within the .beta.-chain of a T-cell antigen receptor; the multidrug resistance (MDR) gene; DNA sequences encoding ribozymes; antisense polynucleotides; genes encoding secretory peptides which act as competitive inhibitors of angiotensin converting enzyme, of vascular smooth muscle calcium channels, or of adrenergic receptors, and DNA sequences encoding enzymes which break down amyloid plaques within the central nervous system. It is to be understood, however, that the scope of the present invention is not to be limited to any particular therapeutic agent.

US-PAT-NO: 5919681

DOCUMENT-IDENTIFIER: US 5919681 A

TITLE: Method for promoting enzyme diversity

----- KWIC -----

Brief Summary Text - BSTX (8):

Recently, however, selection methods have been used to produce catalytic antibodies (see Smiley et al., "Selection of catalytic antibodies for a biosynthetic reaction from a combinatorial cDNA library by complementation of an auxotrophic *Escherichia coli*:antibodies for orotate decarboxylation," 91(18) Proceedings of the National Academy of Sciences of the United States of America 8319-23(1994), which is incorporated herein by reference; Janda et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries," 91(7) Proceedings of the National Academy of Sciences of the United States of America 2532-6), which is incorporated herein by reference. Such methods use selection pressure to isolate antibodies with desired properties instead of the more laborious screening techniques. For example, a catalytic antibody which catalyzes the formation of a cellular growth factor may be selected for in a cell auxotrophic for such growth factor.

US-PAT-NO: 5914256

DOCUMENT-IDENTIFIER: US 5914256 A

TITLE: Method for promoting enzyme diversity

----- KWIC -----

Brief Summary Text - BSTX (8):

Recently, however, selection methods have been used to produce catalytic antibodies (see Smiley et al., "Selection of catalytic antibodies for a biosynthetic reaction from a combinatorial cDNA library by complementation of an auxotrophic Escherichia coli: antibodies for orotate decarboxylation," 91(18) Proceedings of the National Academy of Sciences of the United States of America 8319-23 (1994), which is incorporated herein by reference; Janda et al., "Direct selection for a catalytic mechanism from combinatorial antibody libraries," 91(7) Proceedings of the National Academy of Sciences of the United States of America 2532-6), which is incorporated herein by reference. Such methods use selection pressure to isolate antibodies with desired properties instead of the more laborious screening techniques. For example, a catalytic antibody which catalyzes the formation of a cellular growth factor may be selected for in a cell auxotrophic for such growth factor.

US-PAT-NO: 5892024

DOCUMENT-IDENTIFIER: US 5892024 A

TITLE: Bifunctional nucleosides, oligomers thereof, and methods
of making and using the same

----- KWIC -----

Brief Summary Text - BSTX (4):

An antisense compound binds to or hybridizes with a nucleotide sequence in a nucleic acid (RNA or DNA) to inhibit the function (or synthesis) of the nucleic acid. Because they can hybridize with both RNA and DNA, antisense compounds can interfere with gene expression at the level of transcription, RNA processing or translation. The resulting interference leads to an inhibition of the synthesis of the protein encoded by the nucleic acid, such as the proteins of the tissues, various cellular growth factors, growth factor receptors, and oncogenes.

US-PAT-NO: 5891858

DOCUMENT-IDENTIFIER: US 5891858 A

TITLE: Antisense polynucleotide inhibition of human growth
factor-sensitive cancer cells

----- KWIC -----

Brief Summary Text - BSTX (6):

When these polynucleotides bind to (hybridize with) mRNA, inhibition of protein synthesis (translation) occurs. When these polynucleotides bind to double stranded DNA, inhibition of RNA synthesis (transcription) occurs. The resulting inhibition of translation and/or transcription leads to an inhibition of the synthesis of the protein encoded by the sense strand such as protein of the tissues, and more importantly here, a cellular growth factor, growth factor receptor, oncogene or protooncogene (many of which act as growth factors, receptors or mediators of signal transduction).

US-PAT-NO: 5888765

DOCUMENT-IDENTIFIER: US 5888765 A

TITLE: Endothelial-cell specific promoter

----- KWIC -----

Detailed Description Text - DETX (43):

The endothelial cell-specific promoter sequences of the invention may also be used in gene therapy to promote angiogenesis to treat diseases such as peripheral vascular disease or coronary artery disease. For example, the DNA of the invention can be operably linked to sequences encoding cellular growth factors which promote angiogenesis, e.g., VEGF, acidic fibroblast growth factor, or basic fibroblast growth factor.

US-PAT-NO: 5888762

DOCUMENT-IDENTIFIER: US 5888762 A

See image for Certificate of Correction

TITLE: Neurotropic growth factors comprising a homeobox peptide

----- KWIC -----

Claims Text - CLTX (32):

14. The method according to claim 13, wherein the macromolecule transported into the living cell is a homeobox peptide, which is active as a cellular growth factor.

US-PAT-NO: 5883223

DOCUMENT-IDENTIFIER: US 5883223 A

See image for Certificate of Correction

TITLE: CD9 antigen peptides and antibodies thereto

----- KWIC -----

Detailed Description Text - DETX (84):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0×10^6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5×10^6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0×10^6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 5882894

DOCUMENT-IDENTIFIER: US 5882894 A

TITLE: Nucleic acids encoding CR8 polypeptides, vector and transformed cell thereof, and expression thereof

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 5871961

DOCUMENT-IDENTIFIER: US 5871961 A

TITLE: Nucleic acids encoding CR2 polypeptides, vector and transformed cell thereof, and expression thereof

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 5871960

DOCUMENT-IDENTIFIER: US 5871960 A

TITLE: Nucleic acids encoding CR5 polypeptide, vector and transformed cell thereof, and expression thereof

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones are useful as activators of certain cellular receptors.

US-PAT-NO: 5859206

DOCUMENT-IDENTIFIER: US 5859206 A

TITLE: Antibodies specific for heregulin 2-.alpha.

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

US-PAT-NO: 5858358

DOCUMENT-IDENTIFIER: US 5858358 A

See image for Certificate of Correction

TITLE: Methods for selectively stimulating proliferation of T cells

----- KWIC -----

Detailed Description Text - DETX (84):

Previous known methods to culture T cells in vitro require the addition of exogenous feeder cells or cellular growth factors (such as interleukin 2 or 4) and a source of antigen or mitogenic plant lectin. Peripheral blood CD28.sup.+ T cells were isolated by negative selection using magnetic immunobeads and monoclonal antibodies as described in the Methods and Materials section above. CD4.sup.+ cells were further isolated from the T cell population by treating the cells with anti-CD8 monoclonal antibody and removing the CD8.sup.+ cells with magnetic immunobeads. Briefly, T cells were obtained from leukopheresis of a normal donor, and purified with FICOLL.TM. density gradient centrifugation, followed by magnetic immunobead sorting. The resulting CD28.sup.+, CD4.sup.+ T cells were cultured in defined medium (X-Vivo10 containing gentamicin and L-glutamine (Whittaker Bioproducts) at an initial density of 2.0.times.10.sup.6 /ml by adding cells to culture dishes containing plastic-adsorbed Goat anti-mouse IgG (Kirkegaard and Perry Laboratories, Gaithersburg, Md.) and anti-CD3 mAb G19-4. After 48 hours, the cells were removed and placed in flasks containing either hIL-2 (5%, CalBiochem) or anti-CD28 mAb (500 ng/ml). The cells cultured with IL-2 were fed with fresh IL-2 at 2-day intervals. Fresh medium was added to all cultures as required to maintain a cell density of 0.5.times.10.sup.6 /ml. Cells were restimulated at approximately weekly intervals by culture on plastic-adsorbed anti-CD3 mAb for 24 hours, the cells removed and placed at 1.0.times.10.sup.6 /ml in fresh medium in flasks containing either IL-2 or anti-CD28 mAb.

US-PAT-NO: 5856110

DOCUMENT-IDENTIFIER: US 5856110 A

TITLE: Method of using HRG2-.alpha. to stimulate P185.sup.HeR2

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

US-PAT-NO: 5842477

DOCUMENT-IDENTIFIER: US 5842477 A

TITLE: Method for repairing cartilage

----- KWIC -----

Brief Summary Text - BSTX (16):

According to another preferred embodiment, the preparation of chondrocytes and/or other stromal cells is administered in vivo to the site of the implant after the scaffold and periosteal/perichondrial tissue have been implanted. In yet a further embodiment of the invention, bioactive agents such as cellular growth factors (e.g., TGF-.beta.), factors that stimulate chondrogenesis (e.g., bone morphogenic proteins (BMPs) that promote cartilage formation), factors that stimulate migration of stromal cells and/or matrix deposition, anti-inflammatories or immunosuppressants, are included at the implantation site. For example, these factors can be incorporated into the scaffold material to provide for release at the site of implantation; the scaffold can also be comprised of, or coated with, one or more of these bioactive agents. Alternatively, the factor(s) can be administered into or adjacent to the scaffold, either before, during or after seeding of the stromal cells, e.g., the bioactive agent(s) can be administered to the site, either as a separate preparation or as part of the stromal cell preparation. In addition, the stromal cells seeded at the defect site can be genetically engineered to express the genes for these bioactive agents, e.g., specific types of TGF-.beta. such as TGF-.beta.1 or specific types of BMPs such as BMP-13. Exposure of the defect site to these bioactive agents promotes the successful and/or improved production of new cartilage and/or improves the success of implantation, for example, by reducing the risk of rejection or inflammation associated with the implant.

Brief Summary Text - BSTX (42):

According to one embodiment of the invention, the scaffold may comprise or be modified, e.g., coated or impregnated, prior to implantation with certain substances to enhance the attachment and growth of chondrocytes and other stromal cells on the scaffold in vivo. These substances include, but are not limited to, bioactive agents such as cellular growth factors (e.g., TGF-.beta.), substances that stimulate chondrogenesis (e.g., BMPs that stimulate cartilage formation such as BMP-2, BMP-12 and BMP-13), factors that stimulate migration of stromal cells to the scaffold, factors that stimulate matrix deposition, anti-inflammatories (e.g., non-steroidal anti-inflammatories), immunosuppressants (e.g., cyclosporins), as well as other proteins, such as collagens, elastic fibers, reticular fibers, glycoproteins or glycosaminoglycans, such as heparin sulfate, chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate, keratin sulfate, etc. For example, growth factors such as TGF-.beta., with ascorbate, have been found to trigger

chondrocyte differentiation and cartilage formation by chondrocytes. In addition, hyaluronic acid is a good substrate for the attachment of chondrocytes and other stromal cells and can be incorporated as part of the scaffold or coated onto the scaffold.

Claims Text - CLTX (21):

19. The method of claim 18, wherein the substance is a bioactive agent selected from the group consisting of cellular growth factors, factors that stimulate migration of stromal cells, factors that stimulate chondrogenesis, factors that stimulate matrix deposition, anti-inflammatories, and immunosuppressants.

Claims Text - CLTX (29):

27. The method of claim 26, wherein the substance is a bioactive agent selected from the group consisting of cellular growth factors, factors that stimulate migration of stromal cells, factors that stimulate chondrogenesis, factors that stimulate chondrogenesis, factors that stimulate matrix deposition, anti-inflammatories, and immunosuppressants.

Claims Text - CLTX (38):

36. The method of claim 35, wherein the bioactive agent is selected from the group consisting of cellular growth factors, factors that stimulate migration of stromal cells, factors that stimulate chondrogenesis, factors that stimulate matrix deposition, anti-inflammatories, and immunosuppressants.

Claims Text - CLTX (42):

40. The method of claim 39, wherein the bioactive agent is selected from the group consisting of cellular growth factors, factors that stimulate migration of stromal cells, factors that stimulate chondrogenesis, factors that stimulate matrix deposition, anti-inflammatories, and immunosuppressants.

US-PAT-NO: 5840525

DOCUMENT-IDENTIFIER: US 5840525 A

TITLE: Nucleic acids, vectors and host cells encoding heregulin

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or erb-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu protooncogene has been identified in ethylnitrosourea-induced rat neuroblastomas. The HER2 gene encodes the 1,255 amino acid tyrosine kinase receptor-like glycoprotein p185.sup.HER2 that has homology to the human epidermal growth factor receptor.

US-PAT-NO: 5837536

DOCUMENT-IDENTIFIER: US 5837536 A

TITLE: Expression of human multidrug resistance genes and
improved selection of cells transduced with such genes

----- KWIC -----

Brief Summary Text - BSTX (39):

Heterologous or foreign genes which may be placed into the vectors of the present invention include, but are not limited to genes which encode cytokines or cellular growth factors, such as lymphokines, which are growth factors for lymphocytes. Other examples of foreign genes include, but are not limited to, genes encoding soluble CD4, Factor VIII, Factor IX, ADA, the LDL receptor, ApoI, tumor necrosis factors (TNF's) and ApoC.

US-PAT-NO: 5834229

DOCUMENT-IDENTIFIER: US 5834229 A

TITLE: Nucleic acids vectors and host cells encoding and
expressing heregulin 2-.alpha.

----- KWIC -----

Brief Summary Text - BSTX (6):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or ERB-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu proto-oncogene has been identified in ethylnitrosourea-induced rat neuroblastomas.

US-PAT-NO: 5795752

DOCUMENT-IDENTIFIER: US 5795752 A

TITLE: Method for creating superinduced cDNA library &
isolating ligand-stimulated genes

----- KWIC -----

Brief Summary Text - BSTX (9):

In the method of producing a cDNA library enriched in ligand-inducible genes, a cellular ligand receptor on a cell is activated with a ligand, for a predetermined period of time, to induce expression of those genes expressed as a result of ligand-receptor binding. Useful ligands include any of those which can activate a specific cellular receptor. These include natural or synthetic ligands for the receptor. Ligands include cytokines such as the interleukins, cellular growth factors, colony stimulating factors, hormones, peptides, antibodies, and receptor-binding fragments thereof.

Detailed Description Text - DETX (3):

The method of the invention can be used to create cDNA libraries of the genes induced by activation of a variety of different cellular receptors. The receptors can be cytoplasmic, nuclear, or cell-surface receptors, and include receptors for cytokines, hormones, factors, and peptides. For example, cytokines such as the interleukins (e.g., IL-1 and IL-2), cellular growth factors (e.g., platelet-derived growth factor (PDGF), epidermal growth factor (EGF), fibroblast growth factor (FGF), insulin-like growth factor (IGF)), colony stimulating factors (e.g., multiplication stimulating activity), and hormones (e.g., insulin, somatomedin C, and steroid hormones) are useful as activators of certain cellular receptors.

Claims Text - CLTX (10):

4. The method of claim 3 wherein step (a) comprises treating said cell with a cytokine selected from the group consisting of the interleukins, cellular growth factors, colony stimulating factors, and hormones.

Claims Text - CLTX (70):

31. A cDNA library according to claim 30, wherein said ligand is a cytokine selected from the group consisting of the interleukins, cellular growth factors, colony stimulating factors, and hormones.

US-PAT-NO: 5773246

DOCUMENT-IDENTIFIER: US 5773246 A

TITLE: Methods and compositions useful in the recognition,
binding and expression of ribonucleic acids involved in
cell growth, neoplasia and immunoregulation

----- KWIC -----

Detailed Description Text - DETX (58):

Hel-N1, like HuD, was observed by the inventors to be reactive with an autoantibody present in the sera of patients with paraneoplastic disease, putting it in the category of other human autoantigens that are members of the RRM superfamily (Saitta et al, Rheumatology Clinics of North America, D. Pisetsky, ed., pp. 1-25 (1992)). The potential to bind to oncoprotein mRNAs adds an element of intrigue because these patients are a subset of those inflicted with small lung cell carcinoma in which levels of c-myc protein are elevated. However, the mechanism of initiation of the autoimmune response to these self antigens remains as elusive as that of the systemic snRNP autoantigens. In addition, there is no evidence that Hel-N1 or HuD play a role in the derivation of the paraneoplastic syndrome or of small cell carcinoma. Additional information concerning the influence of Hel-N1 and related proteins on the production of cellular growth factors will be required to argue for such a link.

US-PAT-NO: 5770563

DOCUMENT-IDENTIFIER: US 5770563 A

TITLE: Heparin- and sulfatide binding peptides from the type I repeats of human thrombospondin and conjugates thereof

----- KWIC -----

Brief Summary Text - BSTX (11):

Heparin binding is critical for activities associated with many cellular growth factors, cell adhesion molecules, and certain enzymes involved in the blood clotting cascade. Agents to inhibit these interactions have found numerous uses in prevention of thrombosis. Heparin analogues have been shown to have anti-tumor and antimetastatic activities.

US-PAT-NO: 5756086

DOCUMENT-IDENTIFIER: US 5756086 A

TITLE: Adenoviruses having modified fiber proteins

----- KWIC -----

Brief Summary Text - BSTX (18):

DNA sequences encoding therapeutic agents which may be placed into the adenoviral vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, negative selective markers or "suicide" genes, such as viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 5730970

DOCUMENT-IDENTIFIER: US 5730970 A

TITLE: Pharmaceutical compositions comprising human
interleukin-4 (IL-4)

----- KWIC -----

Brief Summary Text - BSTX (5):

This technology has progressed extremely rapidly in recent years and a variety of exogenous proteins have been expressed in a variety of hosts, but obtaining any desired novel cDNA clone remains an uncertainty. By way of example, some of the eukaryotic proteins produced by recombinant DNA technology include: proinsulin (Naber, S. et al., Gene 21:95-104 [1983]); interferons (Simon, L. et al., Proc. Natl. Acad. Sci. U.S.A., 80:2059-2062 [1983] and Derynck, R. et al., Nucl. Acids Res. 1:1819-1837 [1983]); growth hormone (Goeddel, D., et al., Nature 281:544-548 [1979]); a human T-cell growth factor (Taniguichi, T. et al., Nature 302:305-310 (1983)); and a granulocyte/macrophage cellular growth factor (G/M-CSF) (Miyatake, S. et al., EMBO J. 4:2561-2568 (1985)). These publications and other reference materials cited hereafter have been included to provide additional details on the background of the pertinent art and, in particular instances, the practice of the invention, and are all incorporated herein by reference.)

US-PAT-NO: 5726045

DOCUMENT-IDENTIFIER: US 5726045 A

TITLE: Materials and methods for converting DNA to CO-DNA

----- KWIC -----

Brief Summary Text - BSTX (6):

Several proto-oncogenes are known that encode various cellular growth factors (or growth factor subunits) that are thought to stimulate cell proliferation. When those genes are overexpressed, uncontrolled cell proliferation may result, leading to tumor formation. However, the cellular mechanisms that control cell division in healthy cells versus cancer cells are poorly understood.

US-PAT-NO: 5714478

DOCUMENT-IDENTIFIER: US 5714478 A

TITLE: Sphingosylphosphorylcholine as a wound-healing agent

----- KWIC -----

Brief Summary Text - BSTX (6):

The use of sphingosylphosphorylcholine as a cellular growth factor to increase cell proliferation was disclosed in U.S. Pat. No. 5,374,616, which is incorporated herein by reference. However, that reference does not indicate that sphingosylphosphorylcholine (SPC) can be used for wound healing, a more complex process which requires cell recruitment and tissue remodeling in addition to cell proliferative properties. There are, in fact, many mitotic agents that are not useful for wound healing, including bombesin, bradykinin, insulin and lysophosphatidic acid. For example, data in the cited patent regarding insulin shows that insulin should be used in conjunction with SPC for synergistic effects when simple proliferation enhancement is desired. This combination taught in the prior art is not useful for purposes of wound healing.

US-PAT-NO: 5710037

DOCUMENT-IDENTIFIER: US 5710037 A

TITLE: Retroviral vector particles

----- KWIC -----

Brief Summary Text - BSTX (19):

Genes encoding therapeutic agents which may be placed into such retroviral vector include, but are not limited to, tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 12; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4, Factor VIII, Factor IX, T-cell receptors, the LDL receptor, ApoE, ApoC, the alpha-1 antitrypsin (.alpha.-1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, Fc receptors for antigen-binding domains of antibodies, the insulin gene, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 5707865

DOCUMENT-IDENTIFIER: US 5707865 A

TITLE: Retroviral vectors for expression in embryonic cells

----- KWIC -----

Detailed Description Text - DETX (21):

Nucleic acid sequences encoding therapeutic agents include, but are not limited to, nucleic acid sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding inteferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 15; genes encoding G-CSF, M-CSF, and GM-CSF; genes encoding adenosine deaminase, or ADA; the Zap70 kinase gene; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; the glucocerebrosidase gene; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; the .beta.-globin gene; Factor VIII; Factor IX; T-cell receptors; the .alpha.-iduronidase gene; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene; the ornithine transcarbamylase (OTC) gene; the CFTR gene; the insulin gene; suicide genes such as, for example, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies; antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myb oligonucleotides; multidrug resistance genes such as the MDR-1 gene; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; and selectable markers such as the neomycin resistance (neo.sup.R) gene, the .beta.-galactosidase (lacZ) gene, the chloramphenicol transferase (CAT) gene, and the NGF-R gene.

US-PAT-NO: 5698427

DOCUMENT-IDENTIFIER: US 5698427 A

TITLE: Methods and compositions involved in cell growth,
neoplasia and immunoregulation

----- KWIC -----

Detailed Description Text - DETX (42):

Hel-N1, like HuD, was observed by the inventors to be reactive with an autoantibody present in the sera of patients with paraneoplastic disease, putting it in the category of other human autoantigens that are members of the RRM superfamily (Query et al, Mol. Cell. Biol. (1989), 9:4872-4881). The potential to bind to oncoprotein mRNAs adds an element of intrigue because these patients are a subset of those inflicted with small lung cell carcinoma in which levels of c-myc protein are elevated. However, the mechanism of initiation of the autoimmune response to these self antigens remains as elusive as that of the systemic snRNP autoantigens. In addition, there is no evidence that Hel-N1 or HuD play a role in the derivation of the paraneoplastic syndrome or of small cell carcinoma. Additional information concerning the influence of Hel-N1 and related proteins on the production of cellular growth factors will be required to argue for such a link.

US-PAT-NO: 5693531

DOCUMENT-IDENTIFIER: US 5693531 A

TITLE: Vector systems for the generation of adeno-associated virus particles

----- KWIC -----

Brief Summary Text - BSTX (14):

DNA sequences encoding therapeutic agents which may be placed into the first vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.GAMMA.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4, Factor VIII, Factor IX, T-cell receptors, the LDL receptor, ApoE, ApoC, the alpha-1 antitrypsin (.alpha.-1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 5683894

DOCUMENT-IDENTIFIER: US 5683894 A

TITLE: Recombinant nerve growth factor

----- KWIC -----

Brief Summary Text - BSTX (2):

This invention relates to the molecular biology of cellular growth factors and recombinant DNA technology. More specifically, this invention relates to nerve growth factor (NGF), its therapeutic use, and processes for producing active NGF.

US-PAT-NO: 5681561

DOCUMENT-IDENTIFIER: US 5681561 A

TITLE: Compositions and methods for improving autologous fat
grafting

----- KWIC -----

Brief Summary Text - BSTX (33):

The term "serum free cellular nutrient medium", "serum free cellular nutrient mixture" or "nutrient medium" is used throughout the specification to describe a medium or mixture (generally, at least a minimum essential medium) which contains no serum, and in combination with at least one anabolic hormone, preferably at least two or more anabolic hormones and optionally, at least one cellular growth factor or transforming factor comprises the wound healing compositions according to the present invention. The serum free nutrient medium according to the present invention is a minimum essential medium comprising the following elements: (a) essential amino acids (b) non-essential amino acids; (c) vitamins selected from the group consisting of folate, nicotinamide, pantothenate, pyridoxine, riboflavin, thiamin and mixtures thereof, preferably a vitamin mixture comprising a mixture of folic acid, nicotinamide, pantothenate, pyridoxine, riboflavin and thiamin; (d) glucose or nother equivalent carbon source such as galactose, among others; and (e) a mixture of inorganic ions selected from the group consisting of calcium, sodium, potassium, magnesium, chloride and mixtures thereof, preferably a mixture comprising calcium, sodium, potassium, magnesium and chloride. All of the elements (a), (c), (d) and (e) are necessarily included in a minimum essential medium according to the present invention along with the anabolic hormone. In addition, non-essential amino acids (b) are preferably included in the present compositions. Optionally, the cellular growth factor or transforming factor are also included. All of the elements are included in the medium in concentrations and/or amounts effective for maintaining the growth of lipocytes which are used in the autologous fat grafts of the present invention. The inclusion of non-essential amino acids pursuant to the present invention is clearly preferred. The preferred concentration of essential and optionally and preferably, non-essential amino acids used in the present invention ranges from about 5.0 μm (10.sup.-6 mole) to about 50 mmol. (10.sup.-3 mole). The preferred concentrations of vitamins used in the present invention ranges from about 1 nanomole (10.sup.-9 mol.) to about 10 μm . The preferred concentrations of glucose or equivalent carbon source such as galactose used in the invention ranges from about 1 μmol . to about 10 or more mmol. In the case of element (e), these inorganic ions are preferably included in the present compositions at a concentration range of about 1 μmol to about 50 mmol.

Brief Summary Text - BSTX (37):

The cellular nutrient medium according to the present invention may include

one or more commercially available media in solution or lyophilate (solid) form. The cellular nutrient medium used may be in the form of a lyophilate which is reconstituted with water, preferably sterilized, distilled water prior to use and then supplemented with an anabolic hormone (the anabolic hormone itself optionally in lyophilate form) such as insulin, triiodothyronine, thyroxine, growth hormone or mixtures thereof, and optionally, a cellular growth factor or transforming factor or other additive. Alternatively, the nutrient medium may be used directly in formulations according to the present invention in the form of a solution, or may be formulated first as a lyophilate before being reformulated as a solution prior to use.

Brief Summary Text - BSTX (40):

The term "cellular growth factor", "cellular transforming factor" or "transforming factor" is used throughout the specification to describe those compounds other than the anabolic hormones which may be optionally added to the formulations according to the present invention for their known benefits in stimulating the growth and elaboration of cells. Cellular growth factors or transforming factors for use in the present invention include for example, epithelial growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factor (TGF) and insulin-like growth factor (IGF), among others. In certain formulations according to the present invention, one or more cellular growth factor or transforming factor may be included in combination with at least one anabolic hormone, most preferably a combination of effective amounts of insulin, triiodothyronine and growth hormone in an amount effective for maintaining or enhancing the growth of fat cells which have been injected as part of the autologous fat graft. Cellular growth factors or transforming factors for use in the present invention may include naturally isolated or synthetically produced versions of the above-mentioned compounds or their equivalents and include, where relevant, compounds produced by genetic engineering processes and techniques.

Brief Summary Text - BSTX (47):

The present invention may also optionally include a cellular growth factor or transforming factor in addition to one or more non-steroidal anabolic hormones. Each cellular growth factor or transforming factor is included in the final composition in an effective amount to enhance the growth of lipocytes, i.e., an amount generally ranging from about 0.05 to about 50 ng/ml or higher concentration, and preferably about 1 ng/ml to about 20 ng/ml or more of the final composition.

Brief Summary Text - BSTX (59):

In addition to lipocyte growth effective amounts of non-steroidal anabolic hormones and cellular nutrient media and optionally, effective amounts of at least one cellular growth factor or transforming factor, formulations according to the present invention may also advantageously contain ascorbic acid, which in certain instances may have a beneficial overall effect in maintaining and/or enhancing the growth of lipocytes because of ascorbic acid's ability to function as a reducing agent. Transferrin (which is believed to improve iron transport) in amounts which preferably range from about 500 ng/ml to about 50

ug/ml, more preferably about 5 ug/ml and selenite (preferably, in the form of sodium selenite) in amounts preferably ranging from about 0.5 to about 50 ng/ml, more preferably about 5 ng/ml, may also be optionally included in the present formulations.

Claims Text - CLTX (13):

13. The composition according to claim 2 further including an effective amount of a cellular growth factor or transforming factor selected from the group consisting of epithelial growth factor, transforming growth factor, platelet derived growth factor, insulin-like growth factor and mixtures, thereof.

Claims Text - CLTX (32):

32. The method according to claim 19 further including an adipocyte growth effective amount of a cellular growth factor or transforming factor selected from the group consisting of epithelial growth factor, transforming growth factor, platelet derived growth factor, insulin-like growth factor and mixture, thereof.

Claims Text - CLTX (43):

43. The method according to claim 33 further including an adipocyte growth effective amount of a cellular growth factor or transforming factor selected from the group consisting of epithelial growth factor, transforming growth factor, platelet derived growth factor, insulin-like growth factor and mixtures thereof.

US-PAT-NO: 5643892

DOCUMENT-IDENTIFIER: US 5643892 A

TITLE: Method of treating chronic progressive vascular diseases

----- KWIC -----

Detailed Description Text - DETX (56):

The foregoing data, generated by scientifically validated experimental procedures, demonstrate the effectiveness of PPS in decreasing the synthesis of excess extra- cellular matrix collagen and certain cellular growth factors while increasing the activity of collagen degradation enzymes. These effects indicate that PPS should be highly effective in the clinical management and reversal of scarring-type CPVD.

US-PAT-NO: 5641869

DOCUMENT-IDENTIFIER: US 5641869 A

TITLE: Method for purifying heregulin

----- KWIC -----

Brief Summary Text - BSTX (6):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or erb-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu protooncogene has been identified in ethylnitrosourea-induced rat neuroblastomas. The HER2 gene encodes the 1,255 amino acid tyrosine kinase receptor-like glycoprotein p185.sup.HER 2 that has homology to the human epidermal growth factor receptor.

US-PAT-NO: 5639600

DOCUMENT-IDENTIFIER: US 5639600 A

TITLE: Diagnosis and treatment of cell proliferative disease
having clonal macrophage involvement

----- KWIC -----

Detailed Description Text - DETX (82):

Mutagenesis, including retroviral insertional mutagenesis into the PDGF-B gene, for example, which affects proliferation of the mutagenized macrophages can be used as a diagnostic indicator of clonal macrophage involvement in atherosclerotic disease. Macrophages are recruited to the site of an atherosclerotic lesion and induced to proliferate by PDGF from such sources as platelets, in association with hypercholesterolemia, or shear stress. The discovery disclosed herein of HIV insertion into or near the PDGF-B gene as an inducer of macrophage proliferation suggests that macrophages can be maintained in a clonal (neoplastic) state by mutagenesis (e.g., retroviral insertional mutagenesis); for example, by mutagenesis of a cellular growth factor gene such as PDGF-B.

US-PAT-NO: 5631237

DOCUMENT-IDENTIFIER: US 5631237 A

TITLE: Method for producing in vivo delivery of therapeutic agents via liposomes

----- KWIC -----

Detailed Description Text - DETX (22):

As disclosed herein the genetic therapeutic agents may be oligonucleotides which are specific antisense oligonucleotides. Such antisense oligonucleotides are sequences complementary to mRNA of target genes and may be used for inhibition of expression of the target gene products. Antisense oligonucleotides effectively inhibit gene expression by reducing the amount of mRNA available for translation. In one embodiment of the invention, the antisense oligonucleotides which are transfected via the HVJ-liposome method are designed to inhibit genes that are involved in detrimental vascular conditions, or the formation of such conditions. Those skilled in the art would recognize that the use of one or more antisense oligonucleotides is possible by the methods of the invention. Those skilled in the art will further recognize that such agents may intervene at the level of cell division, cell differentiation, cell growth, cell activation and act on genes which include, but are not limited to, cellular growth factors, cell cycle dependent proteins, cellular kinases, cellular phosphatases, cellular receptors; including FGF, PDGF, ACE, renin, angiotensinogen, TGF-.beta., cdc2 kinase, cdk2 kinase, c-myb, c-myc, c-src, c-lyn, PCNA, cyclin B, and the ANGII receptor. In a preferred embodiment, the treatment of blood vessels for the prevention of restenosis after angioplasty is accomplished by the methods of the invention to transfer antisense oligonucleotides for cdc2 kinase and antisense PCNA into cells of a segment of a blood vessel in vivo via HVJ-liposomes.

Detailed Description Text - DETX (134):

1) In Vitro Transfer of Antisense Oligonucleotides for Cellular Growth Factors for Modification of Cell Growth

US-PAT-NO: 5610288

DOCUMENT-IDENTIFIER: US 5610288 A

TITLE: Antisense polynucleotide inhibition of epidermal human
growth factor receptor expression

----- KWIC -----

Brief Summary Text - BSTX (6):

When these polynucleotides bind to (hybridize with) mRNA, inhibition of protein synthesis (translation) occurs. When these polynucleotides bind to double stranded DNA, inhibition of RNA synthesis (transcription) occurs. The resulting inhibition of translation and/or transcription leads to an inhibition of the synthesis of the protein encoded by the sense strand such as protein of the tissues, and more importantly here, a cellular growth factor, growth factor receptor, oncogene or protooncogene (many of which act as growth factors, receptors or mediators of signal transduction).

US-PAT-NO: 5591709

DOCUMENT-IDENTIFIER: US 5591709 A

TITLE: Compositions and methods for treating wounds

----- KWIC -----

Brief Summary Text - BSTX (18):

The present invention relates to formulations and methods for treating wounds utilizing these formulations. The formulations according to the present invention are useful for treating wounds by accelerating wound healing. These formulations comprise an effective amount of a non-steroidal anabolic hormone selected from insulin, triiodothyronine/thyroxine (T.sub.3 or T₄).sub.4, mixtures thereof, and optionally, growth hormone, most preferably a mixture of all three hormones because of the synergistic effect these three hormones exhibit in combination to promote wound healing, the hormones being further combined with an effective amount of a cellular nutrient medium, preferably a serum free cellular nutrient medium as at least a minimum essential medium, and optionally, at least one cellular growth factor or transforming factor such as insulin-like growth factor (IGF), platelet-derived growth factor (PDGF), epidermal growth factor (EGF) and transforming growth factor (TGF).

Detailed Description Text - DETX (4):

The term "delivery polymer" is used throughout the specification to describe a polymer which can be used in combination with a cellular nutrient medium (preferably, serum free), a non-steroidal anabolic hormone selected from insulin, triiodothyronine, thyroxine, growth hormone and mixtures thereof, and optionally, a cellular growth factor or transforming factor to produce formulations which are preferably used for topical administration to treat wounds according to the present invention. These delivery polymers include, for example, numerous hydrogels in hydrated or unhydrated form, such as those derived from hydroxyethylmethacrylate (HEMA), glycerolmethacrylate (GMA) and polyvinylpyrrolidone (PVP), polyethylene glycol (PEG), various carbohydrates, cellulose and related hydrophilic cellulose polymers, dextran, polyethyleneoxide, dextran-polyethylene, acrylamide, polyacrylamide, amylose, collagen, gelatin, sepharose, agarose (for example, as an agarose saturated gel), related polymers and mixtures thereof, among numerous others. One of ordinary skill in the art will recognize to vary the type and amount of delivery polymer in compositions according to the present invention to provide enhanced wound healing characteristics appropriate for topical delivery. The term delivery polymer is also used to describe polymers which instill slow-release or sustained release characteristics to the wound healing formulations of the invention. The term "gelling agent" is used to describe those polymers which may be included in aqueous formulations according to the present invention in effective amounts to gel these formulations.

Detailed Description Text - DETX (5):

The term "serum free cellular nutrient medium" or "serum free cellular nutrient mixture" is used throughout the specification to describe a medium or mixture (generally, at least a minimum essential medium) which contains no serum, and in combination with at least one anabolic hormone, preferably at least two anabolic hormones and optionally, at least one cellular growth factor or transforming factor comprises the wound healing compositions according to the present invention. The serum free nutrient medium according to the present invention comprises the following elements: (a) essential amino acids; (b) non-essential amino acids; (c) vitamins selected from the group consisting of biotin, folate, lipoate, niacinamide, pantothenate, pyridoxine, riboflavin, thiamin and vitamin B.sub.12 and mixtures thereof, preferably a vitamin mixture comprising folate, niacinamide, pantothenate, pyridoxine, riboflavin and thiamin; (d) glucose; and (e) a mixture of inorganic ions selected from the group consisting of calcium, sodium, potassium, magnesium, chloride and mixtures thereof, preferably a mixture comprising calcium, sodium, potassium, magnesium and chloride. All of these elements (a), (b), (c), (d) and (e) are included with the anabolic hormone and optionally the cellular growth factor or transforming factor in concentrations and/or amounts effective for enhancing the growth of cells which surround, have been injured by or are responsible for healing a wound. The preferred concentration of essential and non-essential amino acids used in the present invention ranges from about 5.0 μM (10^{-6} mole) to about 50 mmol. (10^{-3} Mole) The preferred concentrations of vitamins used in the present invention ranges from about 1 nanomole (10^{-9} mol.) to about 10 μM . The preferred concentrations of glucose used in the invention ranges from about 1 μmol . to about 10 or more mmol. In the case of element (e), these inorganic ions are preferably included in the present compositions at a concentration range of about 1 μmol to about 50 mmol.

Detailed Description Text - DETX (8):

The cellular nutrient medium according to the present invention may include one or more commercially available media in solution or lyophilate (solid) form. The cellular nutrient medium used may be in the form of a lyophilate which may be reconstituted with water, preferably sterilized, distilled water and then supplemented with an anabolic hormone such as insulin, triiodothyronine, thyroxine, growth hormone or mixtures thereof, and optionally, at least one cellular growth factor or transforming factor or other additive. Alternatively, the nutrient medium may be used directly in formulations according to the present invention in the form of a lyophilate, or related solid-type material, rather than a solution, especially when gels, creams, elixirs, powders or other delivery vehicles are to be used for delivery. It is clearly preferred when utilizing solid-type materials for delivering the wound healing compositions according to the present invention that the delivery system in the form of a hydrogel or other form contain moistening quantities of water.

Detailed Description Text - DETX (10):

The term "cellular growth factor" "cellular transforming factor" or "transforming factor" is used throughout the specification to describe those

compounds other than the anabolic hormones which are optionally added to the formulations according to the present invention for their known benefits in stimulating the growth and elaboration of cells. Cellular growth factors or transforming factors for use in the present invention include for example, epithelial growth factor (EGF), platelet derived growth factor (PDGF), transforming growth factor (TGF) and insulin-like growth factor (IGF), among others. In certain preferred formulations according to the present invention, one or more cellular growth factor or transforming factor is included in combination with at least one anabolic hormone, most preferably a combination of effective amounts of insulin, triiodothyronine and growth hormone in an amount effective for stimulating the growth of cells and skin which surround, have been injured by or are responsible for healing a wound. Cellular growth factors or transforming factors for use in the present invention may include naturally isolated or synthetically produced versions of the above-mentioned compounds or their equivalents and include, where relevant, compounds produced by genetic engineering processes and techniques.

Detailed Description Text - DETX (17):

The present invention may also optionally include a cellular growth factor or transforming factor in addition to one or more non-steroidal anabolic hormones. Each cellular growth factor or transforming factor is included in the final composition in an effective amount, i.e., an amount generally ranging from about 0.05 to about 50 ng/ml or higher concentration, and preferably about 1 ng/ml to about 20 ng/ml or more of the final composition.

Detailed Description Text - DETX (18):

In certain embodiments according to the present invention a wound healing composition comprises an effective amount of a cellular growth factor or transforming factor in cellular nutrient medium. PDGF and IGF are preferred growth factors for use in the present invention, with PGDF being most preferred.

Detailed Description Text - DETX (30):

In addition to effective amounts of non-steroidal anabolic hormones and cellular nutrient media and optionally, effective amounts of at least one cellular growth factor or transforming factor, formulations according to the present invention may also advantageously contain ascorbic acid, which in certain instances may have a beneficial overall effect in enhancing wound healing because of its ability to function as a reducing agent. Transferrin (which is believed to improve iron transport) in amounts which preferably range from about 500 ng/ml to about 50 ug/ml, more preferably about 5 ug/ml and selenite (preferably, in the form of sodium selenite) in amounts preferably ranging from about 0.5 to about 50 ng/ml, more preferably about 5 ng/ml, may also be optionally included in the present formulations.

Claims Text - CLTX (5):

5. The formulation according to claim 2 further including an effective amount of a cellular growth factor or transforming factor selected from the group consisting of epithelial growth factor, transforming growth factor,

platelet derived growth factor, insulin-like growth factor and mixtures thereof.

US-PAT-NO: 5552309

DOCUMENT-IDENTIFIER: US 5552309 A

TITLE: Use of polyols for improving the introduction of genetic material into cells

----- KWIC -----

Brief Summary Text - BSTX (38):

DNA sequences encoding therapeutic agents may be placed into the adenoviral vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.gamma.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding epidermal growth factor (EGF), and keratinocyte growth factor (KGF); genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus; antisense c-myb oligonucleotides; and antioxidants such as, but not limited to, manganese superoxide dismutase (Mn-SOD), catalase, copper-zinc-superoxide dismutase (CuZn-SOD), extracellular superoxide dismutase (EC-SOD), and glutathione reductase; tissue plasminogen activator (tPA); urinary plasminogen activator (urokinase); hirudin; nitric oxide synthetase; vasoactive peptides; and angiogenic peptides.

US-PAT-NO: 5552304

DOCUMENT-IDENTIFIER: US 5552304 A

TITLE: CDNA Clones coding for human protein exhibiting a broad cellular activity spectrum (human interleukin-4)

----- KWIC -----

Brief Summary Text - BSTX (5):

This technology has progressed extremely rapidly in recent years and a variety of exogenous proteins have been expressed in a variety of hosts, but obtaining any desired novel cDNA clone remains an uncertainty. By way of example, some of the eukaryotic proteins produced by recombinant DNA technology include: proinsulin (Naber, S. et al., Gene 21:95-104 [1983]); interferons (Simon, L. et al., Proc. Natl. Acad. Sci. U.S.A., 80:2059-2062 [1983] and Derynck, R. et al., Nucl. Acids Res. 1:1819-1837 [1983]); growth hormone (Goeddel, D., et al., Nature 281:544-548 [1979]); a human T-cell growth factor (Taniguichi, T. et al., Nature 302:305-310 (1983)); and a granulocyte/macrophage cellular growth factor (G/M-CSF) (Miyatake, S. et al., EMBO J. 4:2561-2568 (1985)). These publications and other reference materials cited hereafter have been included to provide additional details on the background of the pertinent art and, in particular instances, the practice of the invention, and are all incorporated herein by reference.)

US-PAT-NO: 5547935

DOCUMENT-IDENTIFIER: US 5547935 A

TITLE: Muteins of human epidermal growth factor exhibiting
enhanced binding at low PH

----- KWIC -----

Brief Summary Text - BSTX (3):

This invention relates to the molecular biology of cellular growth factors and recombinant DNA technology. More specifically, this invention relates to epidermal growth factor (EGF) modified to increase its binding activity at low pH, and the therapeutic uses of modified EGF of the invention.

US-PAT-NO: 5543328

DOCUMENT-IDENTIFIER: US 5543328 A

TITLE: Adenoviruses having modified fiber proteins

----- KWIC -----

Brief Summary Text - BSTX (16):

DNA sequences encoding therapeutic agents which may be placed into the adenoviral vector include, but are not limited to, DNA sequences encoding tumor necrosis factor (TNF) genes, such as TNF-.alpha.; genes encoding interferons such as Interferon-.alpha., Interferon-.beta., and Interferon-.delta.; genes encoding interleukins such as IL-1, IL-1.beta., and Interleukins 2 through 14; genes encoding GM-CSF; genes encoding adenosine deaminase, or ADA; genes which encode cellular growth factors, such as lymphokines, which are growth factors for lymphocytes; genes encoding soluble CD4; Factor VIII; Factor IX; T-cell receptors; the LDL receptor, ApoE, ApoC, ApoAI and other genes involved in cholesterol transport and metabolism; the alpha-1 antitrypsin (.alpha.1AT) gene, the ornithine transcarbamylase (OTC) gene, the CFTR gene, the insulin gene, viral thymidine kinase genes, such as the Herpes Simplex Virus thymidine kinase gene, the cytomegalovirus virus thymidine kinase gene, and the varicella-zoster virus thymidine kinase gene; Fc receptors for antigen-binding domains of antibodies, and antisense sequences which inhibit viral replication, such as antisense sequences which inhibit replication of hepatitis B or hepatitis non-A non-B virus.

US-PAT-NO: 5525495

DOCUMENT-IDENTIFIER: US 5525495 A

TITLE: Methods and compositions useful in the recognition,
binding and expression of ribonucleic acids involved in
cell growth, neoplasia and immunoregulation

----- KWIC -----

Detailed Description Text - DETX (58):

Hel-N1, like HuD, was observed by the inventors to be reactive with an autoantibody present in the sera of patients with paraneoplastic disease, putting it in the category of other human autoantigens that are members of the RRM superfamily (Saitta et al, Rheumatology Clinics of North America, D. Pisetsky, ed., pp. 1-25 (1992)). The potential to bind to oncoprotein mRNAs adds an element of intrigue because these patients are a subset of those inflicted with small lung cell carcinoma in which levels of c-myc protein are elevated. However, the mechanism of initiation of the autoimmune response to these self antigens remains as elusive as that of the systemic snRNP autoantigens. In addition, there is no evidence that Hel-N1 or HuD play a role in the derivation of the paraneoplastic syndrome or of small cell carcinoma. Additional information concerning the influence of Hel-N1 and related proteins on the production of cellular growth factors will be required to argue for such a link.

US-PAT-NO: 5444149

DOCUMENT-IDENTIFIER: US 5444149 A

TITLE: Methods and compositions useful in the recognition,
binding and expression of ribonucleic acids involved in
cell growth, neoplasia and immunoregulation

----- KWIC -----

Detailed Description Text - DETX (45):

Hel-N1, like HuD, was observed by the inventors to be reactive with an autoantibody present in the sera of patients with paraneoplastic disease, putting it in the category of other human autoantigens that are members of the RRM superfamily (Query et al, Mol. Cell. Biol. (1989), 9: 4872-4881). The potential to bind to oncoprotein mRNAs adds an element of intrigue because these patients are a subset of those inflicted with small lung cell carcinoma in which levels of c-myc protein are elevated. However, the mechanism of initiation of the autoimmune response to these self antigens remains as elusive as that of the systemic snRNP autoantigens. In addition, there is no evidence that Hel-N1 or HuD play a role in the derivation of the paraneoplastic syndrome or of small cell carcinoma. Additional information concerning the influence of Hel-N1 and related proteins on the production of cellular growth factors will be required to argue for such a link.

US-PAT-NO: 5399352

DOCUMENT-IDENTIFIER: US 5399352 A

TITLE: Device for local drug delivery and methods for using the
same

----- KWIC -----

Detailed Description Text - DETX (51):

Finally, a possible contribution of thrombin to ongoing and late lesion formation is suggested by recent in situ hybridization studies performed on baboon vessels 30 days following carotid artery endarterectomy. At this time point, luminal SMC comprising the neointimal lesion are still actively proliferating as shown by cyclin (PCNA) staining. Interestingly, these same SMC also show good colocalization for both thrombin receptor and PDGF-A chain mRNAs. Thus, these studies demonstrate that vascular repair in the baboon model may be modulated by both cellular growth factors and factors derived from the hemostatic system.

US-PAT-NO: 5378806

DOCUMENT-IDENTIFIER: US 5378806 A

See image for Certificate of Correction

TITLE: Fusion protein produced by retrovirus-mediated secretion

----- KWIC -----

Brief Summary Text - BSTX (4):

Retroviruses are small, membrane-enveloped RNA viruses that were first discovered over 80 years ago. They have been extensively studied because of their importance in helping understand eukaryotic gene expression, their role in elucidating cellular growth factors and oncogenes, their role as human pathogens (particularly in AIDS), and their use as tools to genetically alter host cells, especially for experimental and therapeutic purposes.

(Retrovirology is reviewed by Varmus, 1984, Science 240: 1427-1435). The retrovirus life cycle involves 1) attachment to a host cell via specific receptors, 2) entry into the host, 3) replication of the genomic RNA via a DNA intermediate which then integrates into the host chromosome, 4) transcription and translation of virion genes, 5) assembly of viral components into virion particles and 6) budding of the particles from the plasma membrane. When the virion particle buds from the cell surface, it becomes membrane-enveloped.

US-PAT-NO: 5374616

DOCUMENT-IDENTIFIER: US 5374616 A

TITLE: Compositions containing sphingosylphosphorylcholine and
the use thereof as a cellular growth factor

----- KWIC -----

TITLE - TI (1):

Compositions containing sphingosylphosphorylcholine and the use thereof as
a cellular growth factor

Brief Summary Text - BSTX (3):

The present invention relates to compositions containing
sphingosylphosphorylcholine and the use thereof as a cellular growth factor.

Detailed Description Text - DETX (2):

In accordance with the present invention, it has been surprisingly
discovered that sphingosylphosphorylcholine and pharmaceutical compositions
containing the same exhibit a remarkably potent mitogenic effect for a wide
variety of cell lines. Quite surprisingly, it has been discovered that
sphingosylphosphorylcholine is a much more potent cellular growth factor than
other known growth factors, including sphingosine and sphingosine-1-phosphate,
and also acts synergistically with other agents such as insulin, epidermal
growth factor (EGF), fibroblast growth factor (FGF) and the tumor promoter,
12-O-tetradecanoylphorbol-13-acetate (TPA), to induce cellular proliferation in
mammalian cells.

US-PAT-NO: 5374529

DOCUMENT-IDENTIFIER: US 5374529 A

TITLE: Methods of and compositions for diagnosis, monitoring
and treating the early stages of osteoarthritis

----- KWIC -----

Detailed Description Text - DETX (21):

Another embodiment of this invention provides a therapeutic method and compositions in which the monoclonal antibodies of this invention may be linked to a pharmaceutical drug and administered directly in a pharmaceutically acceptable manner to osteoarthritic lesions. The preferred drug depends on the intended mode of therapeutic application. For example, such a drug might include cellular growth factors, cellular toxins, analogues of cytokine receptors or inhibitors of extracellular proteinases. The dosage and treatment regimens will depend upon factors such as the patient's health status, and the judgment of the treating physician.

US-PAT-NO: 5367060

DOCUMENT-IDENTIFIER: US 5367060 A

See image for Certificate of Correction

TITLE: Structure, production and use of heregulin

----- KWIC -----

Brief Summary Text - BSTX (9):

Among the protooncogenes are those that encode cellular growth factors which act through endoplasmic kinase phosphorylation of cytoplasmic protein. The HER1 gene (or erb-B1) encodes the epidermal growth factor (EGF) receptor. The .beta.-chain of platelet-derived growth factor is encoded by the c-sis gene. The granulocyte-macrophage colony stimulating factor is encoded by the c-fms gene. The neu protooncogene has been identified in ethylnitrosourea-induced rat neuroblastomas. The HER2 gene encodes the 1,255 amino acid tyrosine kinase receptor-like glycoprotein p185.sup.HER2 that has homology to the human epidermal growth factor receptor.

US-PAT-NO: 5357041

DOCUMENT-IDENTIFIER: US 5357041 A

See image for Certificate of Correction

TITLE: Heparin- and sulfatide-binding peptides from the type I
repeats of human thrombospondin

----- KWIC -----

Brief Summary Text - BSTX (4):

Heparin binding is critical for activities in many cellular growth factors, cell adhesion molecules, and certain enzymes involved in the blood clotting cascade. Agents to inhibit these interactions have found numerous uses in prevention of thrombosis. Heparin analogues have been shown to have anti-tumor and antimetastatic activities.

US-PAT-NO: 5334532

DOCUMENT-IDENTIFIER: US 5334532 A

TITLE: PDGF-B fusion protein, vectors, and host cells for use
in production thereof

----- KWIC -----

Brief Summary Text - BSTX (4):

Cellular Growth Factors Generally

Brief Summary Text - BSTX (5):

In recent years, significant attention has been paid to the large number of mitogenic factors, more commonly referred to generically as cellular growth factors, which have been found to be produced by various types of human cells. The outstanding characteristic common to these growth factors is their ability to stimulate proliferation in vitro of a number of cell types. In their normal state, diploid cells in culture rely on the presence of exogenous growth factors to initiate division, and in the absence of these factors, cells will leave the cell cycle and remain in G.sub.1 /G.sub.0 until stimulated externally. On the other hand, transformed cells (e.g., cancerous cells) do not rely upon exogenous growth factors to stimulate mitosis, but rather appear to have some internal control mechanism which permits continuous cell division without any external stimulus. It is in this regard that the so-called "growth factors" have been actively studied. A significant body of evidence suggests that these mitogens may play a role as "transforming proteins" which in vivo are associated with causing the loss of control over growth exhibited by tumor cells. In fact, a number of observations indicate that certain growth factors are routinely made and released by certain human tumor cells in vitro.

US-PAT-NO: 5252559

DOCUMENT-IDENTIFIER: US 5252559 A

See image for Certificate of Correction

TITLE: His-Gly-Gly peptide and derivatives thereof for hair
growth

----- KWIC -----

Detailed Description Text - DETX (118):

The composition according to the invention can also optionally comprise other hair growth stimulants capable of functioning in different ways to enhance the benefit of the hair growth peptide. Examples of other substances with themselves possess the ability to regulate hair growth include, but are not limited to, minoxidil, retinoic acid, diazoxide, Iamin and its derivatives, anti-inflammatories, calcium channel blockers, anti-bacterials, nonionic surfactants, mucopolysaccharides, cellular growth factors, and antiandrogens.

US-PAT-NO: 5175099

DOCUMENT-IDENTIFIER: US 5175099 A

See image for Certificate of Correction

TITLE: Retrovirus-mediated secretion of recombinant products

----- KWIC -----

Brief Summary Text - BSTX (4):

Retroviruses are small, membrane-enveloped RNA viruses that were first discovered over 80 years ago. They have been extensively studied because of their importance in helping understand eukaryotic gene expression, their role in elucidating cellular growth factors and oncogenes, their role as human pathogens (particularly in AIDS), and their use as tools to genetically alter host cells, especially for experimental and therapeutic purposes.

(Retrovirology is reviewed by Varmus, 1984, Science 240: 1427-1435). The retrovirus life cycle involves 1) attachment to a host cell via specific receptors, 2) entry into the host, 3) replication of the genomic RNA via a DNA intermediate which then integrates into the host chromosome, 4) transcription and translation of virion genes, 5) assembly of viral components into virion particles and 6) budding of the particles from the plasma membrane. When the virion particle buds from the cell surface, it becomes membrane-enveloped.

US-PAT-NO: 5158935

DOCUMENT-IDENTIFIER: US 5158935 A

TITLE: Human epidermal growth factor having substitution at
position 11

----- KWIC -----

Brief Summary Text - BSTX (3):

This invention relates to the molecular biology of cellular growth factors and recombinant DNA technology. More specifically, this invention relates to epidermal growth factor (EGF) modified to increase its chemical stability, and the therapeutic uses of modified EGF of the invention.

US-PAT-NO: 4933278

DOCUMENT-IDENTIFIER: US 4933278 A

See image for Certificate of Correction

TITLE: Method of determining the number of cells in cell
culture

----- KWIC -----

Detailed Description Text - DETX (20):

Estimation of the number of fetal bovine endothelial cells as in the foregoing Example 1 is particularly useful in conjunction with measuring the stimulation of cellular growth factors derived from cultured human tumor cells or other sources. See Olander et al., In Vitro 18(2), 99-107 (1982).

US-PAT-NO: 4889802

DOCUMENT-IDENTIFIER: US 4889802 A

TITLE: Enhanced production of recombinant proteins in myeloma cells

----- KWIC -----

Detailed Description Text - DETX (14):

Preferred coding sequences include those encoding enzymes, hormones, lymphokines and cellular growth factors. Examples of such proteins whose genes have been cloned include plasminogen activator, blood clotting factors, growth hormone, luteinizing hormone, insulin, interleukin-1, interleukin-2, alpha-interferon, .beta.-interferon, .gamma.-interferon, tumor necrosis factor, and colony stimulating factor. The coding sequence may also be a "marker" gene, which is used to cotransform a myeloma cell, particularly when the second coding sequence is for a mammalian protein that is not easily detected in an in vitro assay used to screen potential transformants. The marker coding sequence can encode a protein which allows transformed myeloma cells to survive in a selection step which kills myeloma cells not containing the marker sequence. Well known marker genes are known in the art, including, but not limited to, the gene for chloramphenicol acetyltransferase (CAT), neomycin phosphotransferase (neo.sup.R), hypoxanthine phosphoribosyltransferase (hpt), and thymidine kinase (tk). Cells transformed with coding sequences encoding these proteins are able to survive on media which would otherwise be toxic to the cell. Other types of markers, such as .beta.-galactosidase (lacZ), cause cells transformed therewith to change color under certain conditions, thus allowing their selection.

US-PAT-NO: 4695542

DOCUMENT-IDENTIFIER: US 4695542 A

TITLE: cDNA clones coding for polypeptides exhibiting
multi-lineage cellular growth factor activity

----- KWIC -----

TITLE - TI (1):

cDNA clones coding for polypeptides exhibiting multi-lineage cellular growth factor activity

Brief Summary Text - BSTX (11):

In vivo studies on hematopoiesis have shown that a number of soluble cloning stimulating factors (CSF) can regulate the growth of these various progenitor cells. Some of these factors have been partially purified and shown to specifically effect stem cells belonging to a particular cell lineage. For example, erthropoietin stimulates more differentiated members of the erythroid hierarchy (Miyake, T., et.al., J. Biol. Chem. 252: 5558, [1977]), whereas another factor (colony stimulating factor-macrophage or CSF-1) preferentially stimulates macrophage growth in semi-solid cultures of bone marrow cells (Stanley, E., and Heard, P., J. Biol. Chem. 252: 4305, [1977]). Another type of growth factor stimulates hematopoietic colonies consisting of single cell types and mixtures of erythrocytes, megakaryocytes, granulocytes, mast cells and monocyte/macrophages (Iscove, N. et.al., J. Cell. Physiol. Suppl., 1: 65-78, [1982]). The range of progenitor cells responsive to this second type of factor indicates that it may be a multi-lineage cellular growth factor (multi-CSF) effecting various committed progenitor cells, and perhaps pluripotential stem cells as well.

Brief Summary Text - BSTX (17):

The present invention provides cDNA clones coding for polypeptides exhibiting mammalian multi-lineage cellular growth factor activity. A nucleotide sequence for the cDNAs and a putative amino acid sequence for the associated polypeptide are shown in FIG. 1. The cDNA sequence can be integrated into various vectors, which in turn can direct the synthesis of the corresponding polypeptides in a variety of hosts, including eukaryotic cells, such as mammalian cells in culture.

Brief Summary Text - BSTX (18):

More specifically, the invention provides a process for producing a polypeptide exhibiting mammalian multi-lineage cellular growth factor activity, the process comprising the steps of:

Brief Summary Text - BSTX (24):

The mouse cDNA sequence of FIG. 1 is capable of hybridizing with other DNA

sequences, such as DNA coding for mammalian multi-lineage cellular growth factors from a human cDNA or genomic library. It is noted that the described cDNA sequences seem to contain information for a leader region.

Drawing Description Text - DRTX (2):

FIG. 1 illustrates the nucleotide sequence and putative corresponding amino acid sequence of a cDNA clone exhibiting multi-lineage cellular growth factor activity.

Drawing Description Text - DRTX (4):

FIG. 3 illustrates pcD-MCGF, a plasmid carrying a cDNA clone exhibiting mast cell growth factor activity and multi-lineage cellular growth factor activity. Transcription of the 950 bp cDNA insert contained in the pcD expression vector from the SV40 early promoter is indicated by the arrow. The location of the splice donor and acceptor sites are shown. The polyadenylation signal, also derived from SV40, is located at the 3' end of the cDNA insert. The cDNA insert is shaded in black. The remainder of the vector sequences are derived from pBR322, including the .beta.-lactamase gene (Amp.RTM.) and the origin of replication.

Detailed Description Text - DETX (2):

In accordance with the present invention, complementary DNA (cDNA) clones are provided for polypeptides exhibiting mammalian multi-lineage cellular growth factor (multi-CSF) activity. After the cDNA sequences have been incorporated in replicable expression vectors, and the vectors transfected into an appropriate host (e.g., a mammalian cell culture), the expressed polypeptide has the ability to allow the expansion of hematopoietic cells to multiple lineages.

Claims Text - CLTX (1):

1. A process for producing a polypeptide exhibiting mouse multi-lineage cellular growth factor activity, said process comprising the steps of:

PAT-NO: JP02007217422A

DOCUMENT-IDENTIFIER: JP 2007217422 A

TITLE: CONTROL OF GROWTH AND REPAIR OF GASTRO-INTESTINAL TISSUE
BY GASTROKINE AND INHIBITOR

----- KWIC -----

Abstract Text - FPAR (2):

SOLUTION: A novel group of gastrokines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Cytoprotection and control of mammalian gastro-intestinal tissue growth and repair (restoration) is facilitated by the use of the proteins, making the proteins candidates for therapies in inflammatory bowel disease and gastric ulcers.

PUB-NO: WO2007070546A2

DOCUMENT-IDENTIFIER: WO 2007070546 A2

TITLE: MENISCAL IMPLANT OF HYALURONIC ACID DERIVATIVES FOR
TREATMENT OF MENISCAL DEFECTS

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=20070817 STATUS=O>A composite for treating an articular defect includes a hyaluronic acid derivative; and at least one member of the group consisting of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to. the hyaluronic acid derivative. In one embodiment, carboxyl functionalities of the hyaluronic acid derivative are each independently derivatized to include an N-acylurea or O-acyl isourea, or both N-acylurea and O-acyl isourea. In another embodiment, the hyaluronic acid derivative is prepared by reacting an uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer in a range of between about 4 and about 8. The composite can be used for regenerating or stimulating regeneration of meniscal tissues in a subject in need thereof.

PUB-NO: WO2004060476A2

DOCUMENT-IDENTIFIER: WO 2004060476 A2

TITLE: WOUND HEALING METHOD AND KITS

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=20041127 STATUS=O>Electroporation is used to enhance the wound-healing benefit provided by transfection of nucleic acids that encode cellular growth factors. Wounds which are amenable to the method include inter alia cutaneous lesions, muscular lesions, osseous lesions, burn wounds, and gastrointestinal anastomoses. Kits comprise electrodes and nucleic acids encoding cellular growth factors.

PUB-NO: WO003018781A1

DOCUMENT-IDENTIFIER: WO 3018781 A1

TITLE: REGULATION OF CYTOTROPHOBLAST CELL DIFFERENTIATION AND
CELL MIGRATION

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=20030507 STATUS=O>The present invention is predicated on the discovery of certain interactions between cellular growth factors and opposing actions that control differentiation and migration or invasion of cytotrophoblasts into the uterine endometrium during pregnancy. IGF-II and latent transforming growth factor beta (TGF beta), the inactive precursor of TGF beta , compete for binding to the CIM6P receptor. IGF-II prevents latent TGF beta binding to the CIM6P receptor. The invention therefore offers a method of regulating and directing cytotrophoblast differentiation and function based on the interaction between IGF-II, latent TGF beta and the CIM6P receptor. There is disclosed a method of regulating cytotrophoblast and stem cell differentiation and migration characterized by adjusting levels of insulin-like growth factor II (IGF-II) available for binding to the cation-independent mannose-6-phosphate (CIM6P) receptor. The discovery may be applied to embryonic or adult stem cells to control their differentiation and migratory behaviour.

PUB-NO: WO002078640A2

DOCUMENT-IDENTIFIER: WO 2078640 A2

TITLE: CONTROL OF GROWTH AND REPAIR OF GASTRO-INTESTINAL
TISSUES BY GASTROKINES AND INHIBITORS

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=20021101 STATUS=O>A novel group of gastrokines called Gastric Antrum Mucosal Protein is characterized. A member of the group is designated AMP-18. AMP-18 genomic DNA, cDNA and the AMP-18 protein are sequenced for human, mouse and pig. The AMP-18 protein and active peptides derived from it are cellular growth factors. Surprisingly, peptides capable of inhibiting the effects of the complete protein, are also derived from the AMP-18 protein. Cytoprotection and control of mammalian gastro-intestinal tissue growth and repair (restitution) is facilitated by the use of the proteins, making the protein candidates for therapies in inflammatory bowel disease and gastric ulcers.

PUB-NO: EP001172386A1

DOCUMENT-IDENTIFIER: EP 1172386 A1

TITLE: FUNCTIONALIZED GLYCOSAMINOGLYCAN POLYMER AND MEDICAL
INSTRUMENTS AND DRUGS BY USING THE SAME

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=20020202 STATUS=O> The present invention provides a functionalized polymer which can be used extensively in the field of medical drugs as well as medical devices and which is obtainable in an organic synthetic manner from glycosaminoglycan controlling adhesion, migration and proliferation of cells via linkage to various cellular growth factors or cytokines or direct interactions with the cells. The functionalized polymer of the present invention is characterized in that it comprises a carbohydrate corresponding to at least a part of the basic structure of glycosaminoglycan introduced into a vinyl-type polymer chain. <IMAGE>

PUB-NO: WO009118981A2

DOCUMENT-IDENTIFIER: WO 9118981 A2

TITLE: NEUROTROPIC GROWTH FACTORS COMPRISING A HOMEBOX PEPTIDE

----- KWIC -----

Abstract Text - FPAR (1):

CHG DATE=19950211 STATUS=O> New class of cellular growth factors which are active in particular on nerve cells, the said factors comprising at least one homeobox peptide, optionally linked to another peptide sequence.

PUB-NO: WO008603225A1

DOCUMENT-IDENTIFIER: WO 8603225 A1

TITLE: cDNA CLONES CODING FOR POLYPEPTIDES EXHIBITING HUMAN
GRANULOCYTE MACROPHAGE AND EOSINOPHIL CELLULAR GROWTH
FACTOR ACTIVITY

----- KWIC -----

Title of Patent Publication - TTL (1):

cDNA CLONES CODING FOR POLYPEPTIDES EXHIBITING HUMAN GRANULOCYTE
MACROPHAGE
AND EOSINOPHIL CELLULAR GROWTH FACTOR ACTIVITY

DERWENT-ACC-NO: 2007-721458

DERWENT-WEEK: 200768

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Non-therapeutic treatment of mammalian superficial surface of human body part, comprises disposing liquid blood fraction and complex nutritional base, mixing the mixture to obtain active liquid phase and contacting the body part

----- KWIC -----

Basic Abstract Text - ABTX (2):

DESCRIPTION - Method of non-therapeutic treatment of a superficial surface of body part of a mammalian, particularly human being, comprises disposing a liquid blood fraction of the same species of the mammal to be treated, disposing a complex nutritional base (CNB) in aqueous medium, which is distinguished from a cellular culture medium, excludes all cellular growth factor and/or any biological extract of animal or non-traced cell and approaches a cellular culture medium, which allows only a viable culture of epidermic keratinocyte inoculum in vitro, with clonal proliferation of the latter, without live feeder, where the CNB comprises a amino acid fraction of less than 0.5 wt.%, preferably 0.35 wt.%, and a water-soluble vitamins fraction of less than 2 wt.%, preferably 0.015 wt.% and an inorganic fraction of which the trace metal elements and metal salts less than 5%, preferably 2 wt.%, other than the aqueous medium; mixing the liquid blood fraction with the CNB to obtain active liquid phase of local and surface treatment; and contacting the body part to be treated with the active liquid phase. INDEPENDENT CLAIMS are included for:

DERWENT-ACC-NO: 2007-587156

DERWENT-WEEK: 200759

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Treating osteochondral or chondral defect involves
implanting into site of the defect a composite e.g.
scaffold including a hyaluronic acid derivative and
impregnated with a cell or cellular growth factor

----- KWIC -----

Basic Abstract Text - ABTX (1):

NOVELTY - Treating osteochondral or chondral defect in a subject involves implanting a composite in a site of the osteochondral or chondral defect. The composite includes a hyaluronic acid derivative (A1), in which carboxyl functionalities of (A1) are each independently derivatized to include an N-acylurea and/or O-acyl isourea; and at least one member (M1) of the group consisting of a cell, cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to the hyaluronic acid derivative.

Title - TIX (1):

Treating osteochondral or chondral defect involves implanting into site of the defect a composite e.g. scaffold including a hyaluronic acid derivative and impregnated with a cell or cellular growth factor

Standard Title Terms - TTX (1):

TREAT DEFECT IMPLANT SITE COMPOSITE SCAFFOLDING HYALURONIC ACID
DERIVATIVE
IMPREGNATE CELL CELLULAR GROWTH FACTOR

DERWENT-ACC-NO: 2007-587152

DERWENT-WEEK: 200757

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Composite, for treating articular defect comprises specific hyaluronic acid derivative and components of cell, cellular growth factor and cellular differentiation factor which is impregnated in, or coupled to, the hyaluronic acid derivative

----- KWIC -----

Basic Abstract Text - ABTX (1):

NOVELTY - A composite comprises a hyaluronic acid derivative; and at least one component of a cell, a cellular growth factor and a cellular differentiation factor, which is impregnated in, or coupled to, the hyaluronic acid derivative. The carboxyl functionalities of the hyaluronic acid derivative are each derivatized to include an N-acylurea and/or O-acyl isourea.

Title - TIX (1):

Composite, for treating articular defect comprises specific hyaluronic acid derivative and components of cell, cellular growth factor and cellular differentiation factor which is impregnated in, or coupled to, the hyaluronic acid derivative

Equivalent Abstract Text - ABEQ (2):

Preferred Composite: The composite includes at least one component of mesenchymal stem cells, periosteal cells, synoviocytes, fibrochondrocytes, osteochondrocytes, chondrocytes, tumor growth factor-beta (TGFbeta) supergene family components, tissue growth hormones, or their encoding genes or synthetic peptide. The composite is an implantable composite. The composite has interconnected pores of sizes that provide molecular cuing and scaffolding for the impregnated or coupled cell, or path for migration of the cellular growth factor or cellular differentiation factor. The composite additionally includes a biocompatible, biodegradable support, where the hyaluronic acid derivative is at the support. The composite additionally includes a material that enhances adherence of the composite to tissue. The hyaluronic acid derivative is prepared by reacting uncrosslinked hyaluronic acid with a biscarbodimide in the presence of a pH buffer of 4 - 8.

Equivalent Abstract Text - ABEQ (9):

Preferred Device: The device includes a meniscus fibrochondrocyte; and is in the form of a sheet or film that can be cut, trimmed and contoured to fill the meniscal defect in the meniscus. Preferred Method: In the method, the composite include a meniscus fibrochondrocyte. The method additionally

involves stabilizing the composite within the meniscus defect so that the composite does not move during the regenerating or stimulating regeneration of meniscus tissues, where the composite has interconnected 25 pores of sizes that can provide molecular cuing and scaffolding for the impregnated or coupled cell to migrate through, or a path for migration of the impregnated or coupled cellular growth factor or cellular differentiation factor; and fabricating the composite in the shape of the meniscal defect in the meniscus, forming the composite in a sheet or film, and cutting, trimming and contouring the sheet or film to fill the meniscal defect in the meniscus.

Standard Title Terms - TTX (1):

COMPOSITE TREAT ARTICULAR DEFECT COMPRISE SPECIFIC HYALURONIC ACID
DERIVATIVE COMPONENT CELL CELLULAR GROWTH FACTOR DIFFERENTIAL
IMPREGNATE COUPLE

DERWENT-ACC-NO: 2007-475262

DERWENT-WEEK: 200746

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: New liposome composition comprising effector molecule,
useful for treating a condition mediated by binding of
one binding member to a second binding member, e.g.
septic shock

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Composition: The effector molecule is selected from Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, IL-1 inhibitors, ELAM-1 binding inhibitors, or limulus antilipopolysaccharide factor (LALF), where the polysaccharide is sialyl Lewisx, and where the cytokine is selected from interferons (IFNs), interleukins (ILs), tumor necrosis factor (TNF), transforming growth factor beta, lymphotoxin, GM-CSF, or G-CSF. The IFN is IFN-alpha, IFN-beta, or IFN-gamma. The IL is IL-1alpha, IL-113, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, or IL-8.

DERWENT-ACC-NO: 2005-470244

DERWENT-WEEK: 200548

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Use of a complex nutrient medium for skin treatment in humans and animals, e.g. for regenerating skin and promoting wound healing, which is free of growth factors and untraceable animal or cellular products

----- KWIC -----

Basic Abstract Text - ABTX (2):

DESCRIPTION - Use of a complex nutrient base (A), in aqueous medium, to make or obtain a medical composition for topical application to humans or animals. (A) comprises many amino acids, vitamins, trace elements and metal salts but does not contain any cellular growth factors nor untraceable biological extracts of animal or cellular origin. It has at least one of the following characteristics:

DERWENT-ACC-NO: 2005-315706

DERWENT-WEEK: 200821

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: In vitro culturing corneal epithelial cells for transplantation, comprises dissecting corneal endothelial cells, growing in extracellular matrix coated culture plates, passaging cells into a secondary culture system, growing and harvesting

----- KWIC -----

Basic Abstract Text - ABTX (8):

(b) passaging the cells into a secondary culture system (where the secondary culture system is comprised of ECM coated culture plates and the addition of sufficient cellular growth factors);

Basic Abstract Text - ABTX (17):

(c) passaging the cells into a secondary culture system (where the secondary culture system is comprised of an ECM coated culture plates and the addition of sufficient cellular growth factors);

DERWENT-ACC-NO: 2005-122662

DERWENT-WEEK: 200559

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Composition for treating or ameliorating orthopedic or rheumatologic condition, or regenerative connective tissue disease, and repairing cartilage defect, has naked DNA encoding bioactive agent and excipient

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Composition: (I) is further combined with or embedded in a polymeric carrier, biodegradable or biomimetic matrix or a scaffold. In (I), the biodegradable matrix is chosen from polyglycolic acid (PGA), polylactic acid (PLA), hyaluronic acid, catgut suture material, gelatin, cellulose, nitrocellulose, collagen, albumin, fibrin, alginate, cotton or other naturally-occurring biodegradable materials, the scaffold is chosen from nylon (polyamides), dacron (polyesters), polystyrene, polypropylene, polyacrylates, polyvinyl compounds, polycarbonate (PVC), polytetrafluoroethylene (PTFE, teflon), thermanox (TPX), polymers of hydroxy acids such as polylactic acid (PLA), polyglycolic acid (PGA), and polylactic acid-glycolic acid (PLGA), polyorthoesters, polyanhydrides, polyphosphazenes, and polyhydroxyalkanoates and their combinations, and the polymeric carrier is chosen from polymeric mesh or sponge and a polymeric hydrogel. The bioactive agent is chosen from cartilage morphogens and factors or peptides which block inhibitory signals preventing the repair or regeneration of cartilage, or from cellular growth factors, factors that stimulate chondrogenesis, factors that stimulate migration of stromal cells and factors that stimulate matrix deposition. The factor is chosen from an fibroblast growth factor (FGF), transforming growth factor (TGF) and bone morphogenetic protein (BMP), preferably BMP-2.

DERWENT-ACC-NO: 2005-101903

DERWENT-WEEK: 200815

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Preparing autologous cells for preventing and/or treating diseases associated with disturbed self-tolerance, by multiplying monocytes isolated from patients blood in medium containing growth factor and interferon, and separating cells

----- KWIC -----

Basic Abstract Text - ABTX (1):

NOVELTY - Preparing autologous cells for prevention and/or treatment of diseases associated with disturbed self-tolerance in a patient, involves isolating monocytes from blood of patient to whom the cells are to be administered, multiplying the monocytes in a suitable medium containing cellular growth factor, cultivating monocytes in a culture medium containing gamma interferon, and separating the cells from the culture medium.

Basic Abstract Text - ABTX (4):

(b) multiplying the monocytes in a suitable medium containing the cellular growth factor macrophage-colony stimulating factor (M-CSF);

DERWENT-ACC-NO: 2005-020535

DERWENT-WEEK: 200702

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Liposome composition for treating a condition mediated by binding of one binding member (a pathogen in the blood stream) to a second binding member (a target cell), comprises liposomes and effector molecules

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Composition: The effector molecule is Fab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides (sialyl Lewis-x), IL-1 inhibitors, ELAM-1 binding inhibitors and limulus antilipopolysaccharide factor (LALF). The cytokine is interferons (IFN-alpha, IFN-beta or IFN-gamma), interleukins (IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7 or IL-8), tumor necrosis factor, transforming growth factor beta, lymphotoxin, granulocyte macrophage colony stimulating factor (GM-CSF) or granulocyte colony stimulating factor (G-CSF).

DERWENT-ACC-NO: 2004-652784

DERWENT-WEEK: 200577

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Composition useful for treating cancer e.g. lymphoma
comprises chemopotentiating cobalamin drug conjugate or
chemopotentiating nitric oxide donor and optionally
chemotherapeutic agent

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Components: (A2) Is selected from alkylating agents, antimetabolites, anti-tumor antibiotics, taxanes, hormonal agents, monoclonal antibodies, glucocorticoids, mitotic inhibitors, topoisomerase I/II inhibitors, immunomodulating agents, cellular growth factors, cytokines or nonsteroidal anti-estrogenic analogs (preferably cisplatin, carmustine (BCNU), 5-fluorouracil (5-FU), cytarabine (Ara-C), gemcitabine, methotrexate, daunorubicin, doxorubicin, dexamethasone, topotecan, etoposide, paclitaxel, vincristine, tamoxifen, a member of tumor necrosis factor (TNF) superfamily (TNF alpha), Apo2L/TRAIL or interferon beta, especially cytokine, Apo2L/TRAIL or a member of TNF superfamily). (A1) Is nitrosylcobalamin, radiolabeled vitamin B12 homologs, analogs or derivatives, hydroxocobalamin, cyanocobalamin, methylcobalamin or 5-desoxyadenosylcobalamin (preferably nitrosylcobalamin). (A5) Is chemotherapeutic agent, anti-cancer agent or radiation. (A4) Is nitrosylcobalamin, (Z)-1-(2-(2-aminoethyl)-N-(2-aminoethyl)amino)diazen-1-ium-1,2-diolate (NOC-18), S-nitroso-N-acetyl-D,L-penicillamine (SNAP) or sodium nitroprusside (SNP).

DERWENT-ACC-NO: 2004-122937

DERWENT-WEEK: 200833

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Preparing transplant acceptance inducing cells of monocytic origin, useful for suppressing transplant rejection reactions, comprises propagating and cultivating the monocytes in a culture medium containing gamma-interferon

----- KWIC -----

Basic Abstract Text - ABTX (1):

NOVELTY - Preparing transplant acceptance inducing cells of monocytic origin comprises isolating monocytes from blood, multiplying the monocytes in a culture medium containing the cellular growth factor macrophage colony-stimulating factor, cultivating the monocytes, simultaneously with or following the multiplying step, in a culture medium containing gamma-interferon, and separating the cells from the medium.

DERWENT-ACC-NO: 2004-292129

DERWENT-WEEK: 200427

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Method for normalization of cellular growth factors in
men with age androgen deficiency

----- KWIC -----

Title - TIX (1):

Method for normalization of cellular growth factors in men with age androgen
deficiency

Standard Title Terms - TTX (1):

METHOD NORMALISE CELLULAR GROWTH FACTOR MAN AGE ANDROGENIC
DEFICIENT

DERWENT-ACC-NO: 2004-141546

DERWENT-WEEK: 200705

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Liposomes for parenteral administration of small effector molecules such as polypeptides or polysaccharides which are normally subject to rapid renal clearance from the bloodstream

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Liposome: The effector molecule is selected from the group consisting of F.sub.ab antibody fragments, cytokines, cellular growth factors, peptide hormones, monosaccharides, polysaccharides, interleukin (IL)-1 inhibitors, ELAM-1 binding inhibitors, and limulus antilipopolysaccharide factor (LALF). The polysaccharide is sialyl Lewis.sup.x. The cytokine is selected from interferons, interleukins, tumor necrosis factor (TNF), transforming growth factor-beta, lymphotoxin, granulocyte monocyte-colony stimulating factor (GM-CSF), and G-CSF. The interferon is interferon (IFN)-alpha, IFN-beta, or IFN-gamma. The interleukin is IL-1alpha, IL-1beta, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, and IL-8.

DERWENT-ACC-NO: 2003-833539

DERWENT-WEEK: 200830

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Producing dedifferentiated, programmable stem cells of human monocytic origin using culture medium having M-CSF and IL-3, useful in treating cirrhosis, pancreatic insufficiency, kidney failure, cardiac infarction and stroke

----- KWIC -----

Basic Abstract Text - ABTX (1):

NOVELTY - Producing dedifferentiated, programmable stem cells of human monocytic origin, comprises isolating monocytes from human blood, propagating the monocytes in a culture medium which contains the cellular growth factor M-CSF, cultivating the monocytes, subsequently or simultaneously, in a culture medium containing IL-3 and obtaining the human adult dedifferentiated programmable stem cells by separating the cells from the culture medium.

DERWENT-ACC-NO: 2003-618136

DERWENT-WEEK: 200534

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Composition for regenerating organ comprises
cytophysiologically active substance and cells for
transplantation into organ

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Composition: Composition comprises hematopoietic factor, colony stimulating factor or cellular growth factor (preferably fibroblast, hepatocyte or vascular endothelial growth factor and/or compound active at c-met receptors). Cells are vascular cells, bone marrow cells or osteoclasts. Composition also comprises silicone, collagen, gelatin and/or glycolic acid.

DERWENT-ACC-NO: 2003-493306

DERWENT-WEEK: 200464

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Formation of an artificial cartilage useful for treating damaged bone involves delivering a light energy having a specified wavelength to an in vitro culture of a stromal cells and a substrate, and culturing the cells

----- KWIC -----

Equivalent Abstract Text - ABEQ (3):

Preferred Components: The stromal cells are fibroblasts and/or myocytes. (S1) is (a1) used in the preparation of stromal cells and is selected from cellular growth factor, factor that stimulates migration of stromal cells, factor that stimulates chondrogenesis, factor that stimulates matrix deposition, anti-inflammatory agent, and immunosuppressant (preferably transforming growth factor-beta or a bone morphogenetic protein that stimulates cartilage formation, collagen, elastic fiber, reticular fiber, heparin sulfate, chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate, keratin sulfate or hyaluronic acid). (S1) additionally comprises a sustained release formulation. The preparation of stromal cells comprises chondrocyte, chondrocyte progenitor cell, fibroblast and/or fibroblast like cells (preferably a combination of cells selected from chondrocyte, chondrocyte progenitor cell, fibroblast, fibroblast-like cell, endothelial cell, pericyte, macrophage, monocyte, leukocyte, plasma cell, mast cell, adipocyte, umbilical cord cell and bone marrow cells from umbilical cord blood). The chondrocyte progenitor cells comprise mesenchymal stem cells.

DERWENT-ACC-NO: 2003-312691

DERWENT-WEEK: 200461

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Introducing selected molecules to cells of intact organs,
useful e.g. for gene therapy, using a lumen lined with
epithelial or endothelial cells and electroporation

----- KWIC -----

Equivalent Abstract Text - ABEQ (3):

Preferred Molecules: (I) may be a protein or peptide (or nucleic acid encoding it); a drug; antisense polynucleotide or diagnostic reagent. Particularly the nucleic acid is a gene for erythropoietin, factor VIII, elastase inhibitor, protease inhibitor, alpha-1-antitrypsin, cystic fibrosis transmembrane conductance regulator or DNase, operably linked to at least one regulatory element present in a plasmid, which may also contain sequences that allow (non-)homologous recombination into the genome. The drug is a chemotherapeutic, antiinflammatory, diuretic, hormone, immunosuppressant, antibiotic, sulfonamide, antiviral, antiarrhythmic, cardiotonic, vasodilator, anticoagulant, thrombolytic, or antihyperlipemic agent, e.g., digoxin, digitoxin, azathiopine, cyclosporine, antibiotics, sulfonamide, zidovudine, sorsorbide dinitrate, nitroglycerin, calcium channel blockers, beta-blockers, heparin, warfarin, streptokinase, lovostatin, gemfibrozil, pravastatin. (I) may also be a protein (recombinant or synthetic) that facilitates transplantation; reduces transplant rejection; or corrects inborn errors of metabolism or acquired disease, e.g. transforming growth factor beta and/or interleukin-10. The protein may be modified to permit transport to a particular type of cell, especially it linked to a signal peptide, optionally also to a polyanionic peptide to improve water solubility. (I) may also be a wound-healing agent, e.g. a cellular growth factor.

DERWENT-ACC-NO: 2002-434879

DERWENT-WEEK: 200519

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Biocompatible material useful for e.g. controlling
cellular growth comprises at least two component surface

----- KWIC -----

Equivalent Abstract Text - ABEQ (9):

Preferred Components: The first determinant comprises a biologically active compound (b). (a) or (b) comprises a polypeptide, nucleic acid, carbohydrate, and/or lipid. (b) is selected from membrane associated and/or extracellular matrix polypeptides natively produced by a microbial cell, a plant cell or a mammalian cell, a polypeptide (preferably synthetic polypeptide or its part, or adhesive polypeptide, especially fibronectin or vitronectin), antibody, polyclonal antibody, monoclonal antibody, immunogenic determinant, antigenic determinant, receptor, receptor binding protein, interleukine, cytokine, cellular differentiation factor, cellular growth factor or antagonist to a receptor. (e) is a biological cell, virus or their parts, including a polypeptide, nucleic acid, carbohydrate, and/or lipid. (e) is selected from a polypeptide, antibody, polyclonal antibody, monoclonal antibody, immunogenic determinant, antigenic determinant, receptor, receptor binding protein, interleukin, cytokine, differentiation factor, growth factor or antagonist to the receptor. The biological cell or its part is mammalian cell e.g. human cell or animal cell, plant cell, microbial cell e.g. eukaryotic microbial cell such as yeast or fungus, and prokaryotic microbial cell e.g. bacteria (preferably a mammalian cell). The virus or its part is mammalian virus e.g. human or animal virus, plant virus, microbial virus e.g. eukaryotic microbial virus such as yeast virus and fungal virus and prokaryotic microbial virus e.g. bacteriophage (preferably a mammalian virus).

DERWENT-ACC-NO: 2002-113038

DERWENT-WEEK: 200215

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Retroviral vectors resistant to inactivation by human serum, useful to introduce genes into animal cells especially in gene therapy, are produced in a cell line resistant to lysis by human serum

----- KWIC -----

Basic Abstract Text - ABTX (12):

USE - The retroviruses are useful as delivery vehicles to introduce desired genes into animal (especially human) cells, since they are resistant to inactivation by human serum. They are especially useful in gene therapy to introduce polynucleotides encoding endogenous or foreign proteins/polypeptides which may be therapeutic, prophylactic or replacement agents. For example, the polynucleotide included in the retrovirus may encode tumor necrosis factor genes (e.g. tumor necrosis factor α), interferon genes (e.g. interferon α), genes encoding cellular growth factors, a gene encoding a clotting factor to treat e.g. hemophilia. The retroviruses can also be modified by known techniques to increase their effectiveness e.g. the envelope may be modified to target specific cells such as liver cells, or the retrovirus may include negative selectable markers to target tumor cells which are then treated with an interaction agent to kill the cells.

DERWENT-ACC-NO: 2002-194574

DERWENT-WEEK: 200225

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Treatment of septic shock by parenteral administration of liposomes with surface bound polymyxin B which have a much longer circulation time than polymyxin B in free form

----- KWIC -----

Equivalent Abstract Text - ABEQ (8):

(iii) a cytokine or cellular growth factor, for use in stimulating an immune response in the subject;

DERWENT-ACC-NO: 2002-146931

DERWENT-WEEK: 200345

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Parenteral administration of polypeptide or
polysaccharide drugs linked to polyethylene glycol
liposomes to prevent rapid renal clearance from the
bloodstream

----- KWIC -----

Basic Abstract Text - ABTX (14):

(c) stimulating immune responses by administering cytokines or cellular
growth factors;

DERWENT-ACC-NO: 2001-168701

DERWENT-WEEK: 200235

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Producing irreversibly differentiated dendritic cells
from mononuclear cells, useful in immunotherapy of e.g.
cancer, by culturing in presence of specific growth
factors

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Process: Step (i) is for 5 days and step (ii) for 2 days. After step (i) the DC are immature, after step (ii) they are mature. The mononuclear cells are obtained after mobilization with chemotherapeutic agents and/or by using at least one cellular growth factor. The concentrations of GM-CSF, IL and TNF alpha are all 1-1000 ng/ml, particularly 100 ng/ml for GM-CSF and 25 ng/ml for IL, and the amount of HA is 1-2, particularly 2, wt.vol.%

DERWENT-ACC-NO: 2001-168486

DERWENT-WEEK: 200824

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Treating an aneurysm using a biocompatible sleeve, string
or coil for filling the aneurysm

----- KWIC -----

Equivalent Abstract Text - ABEQ (3):

A preferred product comprises a stiff core comprising a hydrogel or wire, surrounded by a soft hydrogel foam overlayed with a water soluble layer (e.g. comprising gelatin). Cellular growth factors, genes, gene products and drugs may be included within the foam or as a coating on the foam.

DERWENT-ACC-NO: 2001-061303

DERWENT-WEEK: 200625

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Expanded polytetrafluoroethylene vascular graft with
increased internodal distance and columnar structure
encourages healing and cellular infiltration

----- KWIC -----

Equivalent Abstract Text - ABEQ (2):

Preferred Device: The fibrils are preferably 50 to 90 microm, especially 55 to 70 microm, long. The internodal space may be partially filled with especially an antibiotic, antimicrobial agent, antineoplastic agent, smooth muscle inhibitor, antithrombotic agent, antiplatelet agent, non-steroidal anti-inflammatory agent, collagen, anti-angiogenesis agent, anti-coagulant or cellular growth factor. The member may be a vascular patch and may be tubular. The tubular graft preferably has a radial tensile strength of at least 0.3 kg/square mm, preferably at least 0.9 kg/square mm.

DERWENT-ACC-NO: 1995-035671

DERWENT-WEEK: 199505

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Novel pharmaceutical compsns. contg.
sphingosyl-phosphoryl-choline used for promoting cellular
proliferation of mammalian cells both in vivo and in
vitro

----- KWIC -----

Basic Abstract Text - ABTX (3):

ADVANTAGE - (I) is a much more potent cellular growth factor than other
known growth factors including sphingosine and sphingosine-1-phosphate and also
acts synergistically with other agents such as (II).

DERWENT-ACC-NO: 1994-316620

DERWENT-WEEK: 200527

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Liposomes for parenteral admin. of polypeptide or polysaccharide attached to outer layer of polyethylene glycol chains, to slow rate of clearance through the kidneys, partic. for polymyxin B used to treat septic shock

----- KWIC -----

Basic Abstract Text - ABTX (3):

USE/ADVANTAGE - The compsns. are used (1) to treat infections (Fab); HIV(CD4); inflammation related to neutrophil recruitment and tissue infiltration (ELAM binders); or septic shock (polymyxin B or its deca-peptide; a specified application); (2) to stimulate the immune response (cytokine or cellular growth factor); (3) to suppress the immune response (IL-1 (receptor) inhibitor); (4) to regulate cell growth (peptide hormone, e.g. parathyroid hormone to inhibit uncontrolled osteoblast division); or (5) to inhibit ligand-receptor cell binding (peptide, e.g. to prevent metastasis). These compsns. provide an effective concn. of (I) in the blood for a relatively long time, e.g. 1-2 days. Also when bound to a liposome, (I) provides greater steric hindrance at the cell surface receptor site. In the case of polymyxin B, attachment to PEG reduces renal accumulation and toxicity.

DERWENT-ACC-NO: 1990-163879

DERWENT-WEEK: 199519

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: Early diagnosis of osteoarthritis by detecting atypical glycosamino-glycan recognised by specific monoclonal antibodies, useful as drug carriers and for monitoring disease

----- KWIC -----

Basic Abstract Text - ABTX (5):

USE/ADVANTAGE - Apart from their use in diagnosis, MAb can be used to monitor the progress of the disease or the effects of drug treatment (particularly for drug screening and development). They may also be used targetting carriers for drugs (e.g. cellular growth factors or toxins) being used to treat osteoarthritic lesions. @ (36pp Dwg.No.1/4)@

DERWENT-ACC-NO: 1986-155831

DERWENT-WEEK: 200460

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: New poly:peptide(s) for colony stimulation of
granulocytes useful for enhancing body defences against
neoplasms and infectious diseases and to overcome
myelo:suppression in chemotherapy

----- KWIC -----

Basic Abstract Text - ABTX (3):

Nucleic acid sequence coding for at least a portion of a polypeptide
exhibiting human granulocyte/macrophage stimulating factor activity and capable
of hybridising to a second nucleic acid sequence coding for another mammalian
cellular growth factor is new.

DERWENT-ACC-NO: 1986-095692

DERWENT-WEEK: 198906

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: New poly:peptide(s) showing murine interleukin-2 activity
are prepd. by recombinant DNA procedures with
complementary DNA clones as vectors in escherichia coli

----- KWIC -----

Basic Abstract Text - ABTX (2):

CDNA clones coding for polypeptides exhibiting murine IL-2 activity are new. Nucleic acid sequence coding for (I) and capable of hybridising to a second nucleic acid sequence coding for another mammalian cellular growth factor is new. Nucleic acid sequence coding for a portion of (I) and capable of hybridising to a second nucleic acid sequence coding for the (I) is new. (5) Vector consisting of the DNA sequence defined in paragraph (4) is new. (6) Replicable vector capable of expressing the DNA sequence defined in paragraph (4) when incorporated into a micro-organism or cell is new. (7) Micro-organism or cell transformed or transfected with a replicable vector as defined in paragraph (6) is new. (8) Transformed organism or cell contg. at least part of a gene or other DNA sequence coding for a polypeptide(s) having murine IL-2 activity is new.

DERWENT-ACC-NO: 1985-100349

DERWENT-WEEK: 199250

COPYRIGHT 2008 DERWENT INFORMATION LTD

TITLE: New poly:peptide(s) having growth factor activities are
prepd. by recombinant DNA procedures

----- KWIC -----

Basic Abstract Text - ABTX (3):

e r Microorganism or cell transformed or transfected with the replicable expression vector is new. Transformed organism or cell contg. at least a portion of a gene or other DNA sequence coding for a polypeptide(s) having mammalian multi-lineage cellular growth factor activity and/or mammalian mast cell growth factor is new. Recombinant DNA molecule contg. a DNA sequence coding for (I) sequence, a DNA sequence Ly to it and codes for the growth factors and DNA sequences that on expression code for a protein showing the growth factor activity. Mammalian IL-3 free from other mammalian proteins is new.

Basic Abstract Text - ABTX (4):

USE/ADVANTAGE - The polypeptides obtd. have multi-lineage cellular growth factor and/or mast cell growth factor activities, and they are used for therapeutic purposes. The cDNA clones provide accurate and complete sequence data for the growth factors.